UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION	MDL No. 2804
	Case No. 17-md-2804
This document relates to:	Hon. Dan Aaron Polster
The County of Summit, Ohio, et al. v. Purdue Pharma L.P., et al. Case No. 18-op-45090	
The County of Cuyahoga, Ohio, et al. v. Purdue Pharma L.P., et al. Case No. 17-op-45004	

Expert Report of Jonathan Ketcham, PhD

May 10, 2019

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I. Qualifications

1. I am the Earl G. and Gladys C. Davis Distinguished Research Professor in Business at the W.P. Carey School of Business at Arizona State University. I am also a Faculty Affiliate in the Department of Economics at the W.P. Carey School of Business at Arizona State University. Prior to joining Arizona State University, I was a Robert Wood Johnson scholar in the Health Policy Research Program at the University of California, Berkeley. I received my Ph.D. in Economics from the Wharton School of Business of the University of Pennsylvania in 2002, and hold a B.A. degree in Economics from Baylor University.

2. At Arizona State University, I teach courses in Health Care Economics and Marketing Research to undergraduates and MBA students. I have published peer-reviewed academic articles in top economics and health policy journals such as the *American Economic Review* and *Health Affairs*, and I have been invited to present my research at a number of conferences and seminars. My research relies on econometrics and economic theory to evaluate the roles of information and incentives in health care. For example, some of my prior work analyzed large data sets to determine how consumers choose insurance plans and how physicians choose drugs and other treatments for their patients. For my work, I have received awards such as the university-wide award for the Best Application of Defining Edge Research and Creative Work from Arizona State University, as well the National Institute for Health Care Management ("NIHCM") Foundation Health Care Research Award. My research has also been funded by a number of large federal grants. A copy of my curriculum vitae, including my prior testimony, is attached to this report as **Exhibit 1**.

3. For my work on this matter, I am being compensated at a rate of $775 per hour. In the preparation of this report, I have been assisted by staff of Cornerstone Research, who worked under my direction. My compensation for work on this matter is not contingent in any way upon the content of my opinions or the outcome of litigation in this or any other matter.

II. Brief Overview of Certain Allegations and Assignment

4. Plaintiffs assert claims against multiple Defendants.[1] I have been retained by counsel for and offer opinions on behalf of Teva Pharmaceuticals USA, Inc. ("Teva USA"), Cephalon, Inc. ("Cephalon"), Actavis Pharma, Inc. ("Actavis Pharma"), Actavis LLC ("Actavis LLC"), Watson Laboratories, Inc. ("Watson"), Anda, Inc. ("Anda"), and their affiliates.[2] I also offer my general (non-company-specific) opinions on behalf of the Mallinckrodt and Janssen Defendants.

5. Teva USA became affiliated with Cephalon in October 2011.[3] Teva USA and Cephalon, at times have manufactured and/or sold two branded opioid products, Actiq and Fentora.[4] Both products have fentanyl citrate as the active ingredient, but they differ in their delivery mechanism.[5] Both products are "indicated for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain."[6] Teva USA also manufactures and sells generic versions of opioids.[7] Additional Defendants include the Actavis Generic Defendants, which manufacture generic opioids,[8] along with Anda,[9] the Mallinckrodt Defendants,[10] and the Janssen Defendants.[11]

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[1] Second Amended Corrected Complaint and Demand for Jury Trial, *The County of Cuyahoga et al. v. Purdue Pharma L.P. et al*, May 18, 2018 ("Cuyahoga Complaint"); Third Amended Complaint and Jury Demand, *The County of Summit et al. v. Purdue Pharma L.P. et al*, March 21, 2019. ("Complaint") Teva USA and Cephalon are referred to as the "Teva Defendants."

[2] Teva USA and Cephalon are referred to as the "Teva Defendants." Actavis Pharma, Actavis LLC, Watson, Warner Chilcott Company, LLC, Actavis South Atlantic LLC, Actavis Elizabeth LLC, Actavis Mid Atlantic LLC, Actavis Totowa LLC, Actavis Kadian LLC, Actavis Laboratories UT, Inc. f/k/a Watson Laboratories, Inc.-Salt Lake City, and Actavis Laboratories FL, Inc., f/k/a Watson Laboratories, Inc.-Florida are referred to as the "Actavis Generic Defendants." In addition, I understand that Teva Pharmaceutical Industries, Ltd. ("Teva Ltd.") has been named as a defendant in this case based upon the conduct of the Teva and Actavis Generic Defendants, but contests personal jurisdiction. The opinions stated herein as to the Teva and Actavis Generic Defendants also apply to Teva Ltd.

[3] Teva Press Release, "Teva Completes Acquisition of Cephalon," October 14, 2011.

[4] Complaint, ¶ 70.

[5] FDA, Actiq Label, November 4, 1998 ("Original Actiq Label, 1998"), pp. 1–2; FDA, Fentora Label, September 25, 2006 ("Original Fentora Label, 2006"), p. 2

[6] Original Fentora label, 2006, p.1. I note the very similar indication for Actiq. See Original Actiq label, 1998, p. 1. These indications have not been altered except to specify minimum ages.

[7] Complaint, ¶ 70.

[8] Complaint. ¶¶ 49–66.

[9] Complaint, ¶ 103.

[10] Complaint ¶ 94.

[11] Complaint, ¶ 72.

6. Plaintiffs allege that the Teva and Actavis Generic Defendants and certain other manufacturers (the "Marketing Defendants") increased sales of opioids over the period 1995–the present ("the period of the allegations")[12] by illegally misrepresenting to physicians the risks, benefits, and appropriateness of long-term use of these medications.[13]

7. Moreover, Plaintiffs allege that Marketing Defendants were also involved in the oversupply of opioids because they failed to have effective controls over the distribution of prescription opioids.[14] According to Plaintiffs, Marketing Defendants knew that the quantities of prescription opioids could not be used for legitimate medical reasons and they failed to report and halt these suspicious orders.[15]

8. More specifically, with respect to allegations related to marketing practices,[16] the *Summit* Complaint asserts that Marketing Defendants allegedly made false and misleading statements about opioids, including that the risk of addiction from chronic opioid therapy is low; to the extent there is a risk of addiction, it can be easily identified and managed; long-term opioid use improves functioning; and others.[17] Plaintiffs allege that these falsehoods were disseminated through multiple channels, including patient advocacy groups and professional associations, key opinion leaders, detailing, and others.[18]

9. I have been retained by counsel for the Teva Defendants and the Actavis Generic Defendants to evaluate the knowledge and policies of informed actors related to opioid medicines manufactured by these entities and the effects that such policies had on opioid utilization and consequences thereof. I also have been asked to review and comment on the expert reports submitted by Professor Meredith Rosenthal ("the Rosenthal Report") and by Professor Jonathan Gruber ("the Gruber Report") on March 25, 2019. In particular, I have been asked to evaluate the analysis of the causal relationship between the alleged misconduct related to marketing and the alleged harm that is set forth in these two expert reports.

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[12] Complaint, ¶¶ 22, 152, 293.
[13] Complaint, ¶¶ 9–12.
[14] Complaint, ¶ 14.
[15] Complaint, ¶ 14.
[16] Anda is not a "Marketing Defendant." Moreover, neither Professor Rosenthal nor Professor Gruber specifically address Anda in their reports or opinions. To the extent Plaintiffs purport to offer any of these opinions generally as to Anda, they are flawed for substantially the same reasons expressed herein.
[17] Complaint, ¶ 172.
[18] Complaint, ¶. 345–459.

10. In the process of preparing this report, I have reviewed a variety of documents, including academic literature, public documents and data from different sources. A complete list of the documents I have considered in forming my opinions is attached as **Exhibit 2**.

11. I reserve the right to supplement or amend my opinions in light of additional information received after the submission of this report.

III. Summary of Opinions

12. The risks of opioids in general, and of the Teva and Actavis Generic Defendants' opioids in particular, were generally known, or should have been known, to informed actors, including the Plaintiffs, in the U.S. during the period of the allegations. The FDA and DEA were aware of such risks; the FDA demonstrated awareness through its adoption of risk mitigation programs for certain opioids and through its labeling decisions, while the DEA demonstrated awareness through assigning most opioids to Schedule II almost immediately upon passage of the Controlled Substances Act in 1970. Health insurers and other third party payors ("TPPs") should also have been aware of these risks given their roles in making decisions about pharmacy benefits for their enrollees.

13. Plaintiffs and Plaintiffs' experts do not appropriately consider the role that TPPs have in influencing the prescribing and use of opioid drugs, as well as TPPs' financial incentives to encourage opioid use. In particular, TPPs and the State of Ohio could have more aggressively utilized the tools at their disposal to manage opioid prescribing and the risks thereof, but did not do so. Such tools include, but are not limited to, prior authorization requirements, step therapy requirements, quantity limits, prescription drug monitoring programs, and policies toward naloxone and other medication assisted therapy ("MAT") for opioid use disorder ("OUD"). Academic evidence demonstrates that these tools affect prescribing behavior in general, and opioid abuse in particular. Plaintiffs and Plaintiffs' experts also ignore the financial incentives that TPPs had to cover opioids over other methods of treating pain.

14. Professor Gruber has failed to establish a causal relationship between opioid shipments and opioid abuse and mortality. His conclusions fail to account for a host of other factors, often acknowledged by Professor Gruber himself that can influence opioid abuse. For example,

Professor Gruber does not consider the role of socioeconomic and macroeconomic factors or the role of health insurance coverage in affecting opioid abuse.

15. Professor Gruber makes several unsubstantiated claims regarding the linkage between prescription opioid shipments and the use of illicit opioids. He fails to acknowledge the important differences between medical and nonmedical use of prescription opioids, and how these difference are related to future illicit opioid use. He also fails to establish a causal link between the Marketing Defendants alleged false marketing conduct and non-medical use of prescription opioids. Professor Gruber lists multiple factors that contributed to illicit opioid use, yet implies that Marketing Defendants are primarily responsible. These factors include, for example, the lower price of heroin and the entry of fentanyl into the U.S. from China and Mexico. Moreover, Professor Gruber assumes, without providing any evidence, that there is a "stock of individuals susceptible to illicit opioid use and abuse."[19] Furthermore, while Professor Gruber considers licit and illicit opioids to be substitutes, he does not quantify the extent to which individuals substituted between the two prior to 2010.

16. Professor Rosenthal's two main analyses (the "direct approach" and the "indirect approach") suffer from multiple flaws and consequently cannot reliably establish a causal relationship between Defendants' alleged promotion of opioids and opioid shipments. They also cannot reliably establish a causal relationship with regards to the Teva and Actavis Generic Defendants' alleged promotion of opioids and opioid shipments.

17. Professor Rosenthal's "direct approach" is flawed and consequently cannot reliably establish a causal relationship between Defendants' alleged promotion and opioid shipments.

- The direct approach fails well-established validation tests. Using Professor Rosenthal's model and chosen interpretation, we would conclude that 1) a randomly generated sequence of numbers causes opioid shipments to virtually the same extent as actual opioid detailing; 2) opioid detailing causes changes in the price of gold; and 3) detailing prior to March 2002 alone causes virtually all of the opioid shipments for the period 1995–2018. These results show that Professor Rosenthal's model cannot be used to support her conclusion that the stock of detailing causes opioid shipments.

[19] Gruber Report, ¶ 16.

- The positive correlation between Professor Rosenthal's stock of detailing and opioid shipments is related to the negative depreciation rate on the past stock of detailing as well as the linearly decreasing coefficient on detailing for the period when opioid shipments are decreasing. However, a negative depreciation rate related to detailing is illogical and contradicted by the academic literature. When the depreciation rate is fixed at reasonable, positive values, Professor Rosenthal's direct approach yields results that contradict her conclusions.
- Professor Rosenthal's direct approach does not distinguish between lawful and unlawful promotions. These effects of lawful and unlawful promotion need not be the same, and some evidence in other contexts has found that false advertising may reduce sales. Similarly, Professor Rosenthal does not consider the various factors that would cause different manufacturers' promotions to have a different impact on opioid sales. Instead, she assumes that all manufacturer Defendants' promotions have the same impact on opioid sales conditional on the timing of those promotions and the price index used by Professor Rosenthal.
- Professor Rosenthal's direct approach is further invalidated by simultaneity bias, reverse causality, and measurement error for price. For example, Professor Rosenthal ignores a number of factors—unrelated to the alleged activities of Marketing Defendants—affecting opioid prescribing. These include, among other things, health plan coverage decisions, patient characteristics, and drug life cycle effects.
- Professor Rosenthal's construction of the but-for world is inappropriate because she implausibly assumes, without providing any support, that 1) all of Defendants' detailing activities were unlawful from 1995 onward; 2) but for the alleged misconduct, Defendants would not have detailed physicians at all for their opioid products.

18. Professor Rosenthal's "indirect approach" using the "residual method" is flawed conceptually and in implementation and cannot reliably establish the effects of alleged unlawful promotion.

- Her model fails to account for well-known factors that systematically affect opioid MMEs. These include technological change, expansion of prescription drug insurance coverage generally and for opioids specifically, the interaction between technology and insurance coverage, changing disease prevalence, and unmeasured changes in socioeconomic and demographic factors. Her failure to account fully for these relevant factors precludes her ability to interpret the residual as the causal effect of alleged unlawful promotion.
- Professor Rosenthal's indirect approach is composed of three components—the cross-sectional regression of 1997, the adjustment for a linear secular trend, and the incorporation of the price index coefficient from the direct approach—each of which is incorrectly estimated.
- Professor Rosenthal asserts that "detailing is a good proxy for total promotional effort." Assuming this assertion is correct, then a strong, positive correlation should exist between the excess MMEs from her indirect approach and detailing stocks. However, the correlation between the excess opioid shipments calculated by the indirect approach and the stock of detailing calculated by her direct approach, when using proper depreciation rates, are low: the correlation coefficients are from 0.28% to 12.01%, failing to support Professor Rosenthal's conclusion that her estimated excess MMEs are the result of marketing.

19. Professor Rosenthal's calculations of MME growth due to under-treated pain are based on certain assumptions about the pain conditions for which opioids are properly indicated. These assumptions are contradicted by Dr. Michna and Dr. Rosenblatt, who state that opioids can be appropriate and effective for treating chronic non-cancer pain under certain circumstances. Professor Rosenthal also does not consider other factors that may cause opioid MMEs to increase. These issues render Professor Rosenthal's analysis of under-treated pain is unreliable.

IV. The Risks of Opioid Abuse Were Generally Known, or Should Have Been Known, to Informed Actors during the Period of the Allegations

A. During the Period of the Allegations, the Risks of Opioids Were Widely Known Across the U.S.

20. The potential for diversion of and dependence on opioids has been understood by the medical and public health communities since at least the early 20th century. For example, "[i]n 1914, the Harrison Narcotics Tax Act imposed a tax on those making, importing or selling any derivative of opium or coca leaves. By the 1920s, doctors were aware of the highly addictive nature of opioids and tried to avoid treating patients with them. Heroin became illegal in 1924."[20] The DEA assigned most opioids to Schedule II almost immediately upon the passage of the Controlled Substances Act in 1970.[21]

21. In the years since, studies of the various drugs' efficacies have been commissioned, and their results disseminated publicly. Thus, reasonably informed actors were or should have been generally aware of these issues during the period of the allegations. In this section, I discuss some of the information that was publicly available and show that many informed agents were aware of such information. Sources of information include reports from various public outlets, as well as academic medical literature.

22. One example is the "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain" (the "Model Guidelines"), which have been available since early 1998.[22]

> These materials emphasize the need to properly evaluate patients and help teach physicians about proper documentation and alert them to the possibilities of abuse and diversion at the same time that proper pain management is emphasized. The Model Guidelines were approved by the Federation of State Medical Boards of the United States in May of 1998 after development by a blue ribbon panel and with the support of the American Academy of Pain Medicine, the American Pain

[20] Sonia Moghe, "Opioid History: From 'Wonder Drug' to Abuse Epidemic," *CNN*, October 14, 2016, available at https://www.cnn.com/2016/05/12/health/opioid-addiction-history/index.html, accessed January 29, 2019.
[21] "Schedules of Controlled Substances," *Federal Register* 36, no. 80, April 24, 1971, pp. 7802–7812, p. 7804.
[22] Model Policy for the Use of Controlled Substances for the Treatment of Pain," Federation of State Medical Boards of the United States, Inc. Report, May 2004 ("Model Guidelines"), p. 1.

Society, the American Society of Law, Medicine and Ethics, and the University of Wisconsin Pain and Policy Studies Group.[23]

23. The guidelines extensively discuss the risks of opioid abuse, and highlight the importance of managing this risk:

- "All physicians should become knowledgeable about…effective methods of pain treatment, as well as statutory requirements for prescribing controlled substances."[24]
- "The Board recognizes that…inappropriate prescribing of controlled substances, including opioid analgesics, may lead to drug diversion and abuse by individuals who seek them for other than legitimate medical use. Accordingly, the Board expects that physicians incorporate safeguards into their practices to minimize the potential for the abuse and diversion of controlled substances."[25]
- "All such prescribing [of controlled substances] must be based on clear documentation of unrelieved pain…Compliance with applicable state or federal law is required."[26]
- "The physician should discuss the risks and benefits of the use of controlled substances with the patient…The patient should receive prescriptions from one physician and one pharmacy whenever possible. If the patient is at high risk for medication abuse or has a history of substance abuse, the physician should consider the use of a written agreement between physician and patient outlining patient responsibilities."[27]
- "Special attention should be given to those patients who are at risk for medication misuse, abuse or diversion. The management of pain in patients with a history of substance abuse or with a comorbid psychiatric disorder may require extra care,

[23] "Oxycontin: Balancing Risks and Benefits," Senate Hearing of the Committee on Health Education, Labor, and Pensions, No. 107-287, available at https://www.gpo.gov/fdsys/pkg/CHRG-107shrg77770/html/CHRG-107shrg77770.htm ("Senate Hearing No. 107-287"), p. 70.
[24] Model Guidelines, p. 2.
[25] Model Guidelines, p. 3.
[26] Model Guidelines, p. 3.
[27] Model Guidelines, p. 4.

> monitoring, documentation and consultation with or referral to an expert in the management of such patients."[28]

24. In 2002, the United States Senate Committee on Health, Education, Labor and Pensions conducted a hearing on OxyContin, discussing opioid misuse and abuse and its consequences at one of the highest levels in national governance and politics.[29] The hearing included testimony from the FDA director of the Office of New Drugs about the FDA's efforts to control the abuse and misuse of OxyContin, including implementing labelling changes, physician and pharmacist outreach efforts, and the FDA's work with the DEA to address illegal diversion of OxyContin.[30] A director at the Substance Abuse and Mental Health Services Administration also testified regarding the treatment gaps for "opioid addiction," as well as the unique facets of OxyContin leading to high rates of abuse, including OxyContin's high levels of active ingredient, and the profitability of diverting the drug on the black market.[31] The committee received anecdotal evidence about OxyContin's impact on opioid abuse from a doctor in Lee County, Virginia, who called it the "fastest growing epidemic of prescription drug abuse in the U.S. in the last 25 years."[32] Later, a representative reading a prepared statement on behalf of CVS outlined OxyContin's "high potential for abuse" for the Senators, and stated that societal issues like "[i]nappropriate prescribing, prescription fraud, prescription rings engaging in 'Doctor Shopping,' employee thefts, increased number of evening break-ins, and armed robberies, have been the direct result of the abuse of OxyContin."[33] These high profile proceedings should have served to further disseminate information about the risks associated with opioid drugs.

25. Another example is the Drug Effectiveness Review Project ("DERP"), run by the Oregon (now Pacific Northwest) Evidence-based Practice Center at Oregon Health & Science University. According to the Center's website, the DERP "was initiated in 2003…to inform evidence-based decisions about drugs…Because the investigators have direct, regular

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[28] Model Guidelines, p. 4.
[29] Senate Hearing No. 107-287.
[30] Senate Hearing No. 107-287, pp. 14–18.
[31] Senate Hearing No. 107-287, pp. 24–28.
[32] Senate Hearing No. 107-287, pp. 43–44.
[33] Senate Hearing No. 107-287, p. 98.

communication with policy-makers at participating Medicaid agencies, the reports have direct impact on policy and decision-making."[34]

26. In fact, before the name DERP had been minted, the entity published a report on long-acting opioid analgesics for chronic non-cancer pain.[35] That report's introduction notes that opioids "are the most potent medications available for treatment of most types of severe pain," but that they are also "associated with…abuse and addiction."[36] The subcommittee that commissioned the study "specifically requested that we examine whether opioids differ in the risk of abuse and addiction."[37] There were no conclusive findings on which opioids have the largest problems with abuse,[38] but the report served to make policy makers aware of such problems.

27. Several states have pooled their resources and participate in DERP, obtaining immediate access to all of the Project's findings.[39] However, until this year, the State of Ohio (an important payor in Ohio through the Medicaid program[40]) did not participate, and therefore did not obtain immediate access to these findings.[41]

28. Other similar entities also have disclosed data and information to try to inform prescribers and policy makers about problems with opioid abuse. For example, "[i]n 2006, the CDC initiated efforts to better track and understand data related to the growing opioid overdose

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[34] "Drug Effectiveness Review Project (DERP)," *Pacific Northwest Evidence Based Practice Center*, available at https://www.ohsu.edu/xd/research/centers-institutes/evidence-based-practice-center/drug-effectiveness-review-project/index.cfm, accessed January 21, 2019.
[35] Roger Chou and Elizabeth Clark, "Drug Class Review on Long-Acting Opioid Analgesics for Chronic Non-Cancer Pain," Oregon Evidence-based Practice Center, November 2002 ("DERP 2002"), p. 3.
[36] DERP 2002, p. 3.
[37] DERP 2002, p. 5.
[38] DERP 2002, pp. 13-16.
[39] "Drug Effectiveness Review Project (DERP)," *Pacific Northwest Evidence Based Practice Center*, available at https://www.ohsu.edu/xd/research/centers-institutes/evidence-based-practice-center/drug-effectiveness-review-project/index.cfm, accessed January 21, 2019.
[40] See Sections V.A and V.B for discussions of Ohio Medicaid.
[41] "Drug Effectiveness Review Project (DERP)," *Pacific Northwest Evidence Based Practice Center*, available at https://www.ohsu.edu/xd/research/centers-institutes/evidence-based-practice-center/drug-effectiveness-review-project/index.cfm, accessed January 21, 2019; "Drug Effectiveness Review Project (DERP)," *Pacific Northwest Evidence Based Practice Center*, available at https://www.ohsu.edu/xd/research/centers-institutes/evidence-based-practice-center/drug-effectiveness-review-project/index.cfm, accessed May 2, 2019.

epidemic."[42] Since then, the CDC has provided data and reports at regular intervals to allow policy-makers to have an understanding of the benefits and downsides to opioids.[43]

29. The Academy of Managed Care Pharmacy ("AMCP") has been active in disseminating knowledge about opioid abuse. The AMCP is "the nation's leading professional association dedicated to increasing patient access to affordable medicines, improving health outcomes, and ensuring the wise use of health care dollars."[44] According to a recent article, "a growing number of organizations have begun implementing formulary guidelines issued by the AMCP."[45] As an example of their activities disseminating knowledge about the risks of opioids, the Academy hosted a research symposium in 2016 entitled *Balancing Access and Use of Opioid Therapy* that focused on many topics, including abuse.[46] That symposium recognized the role that many entities play, noting that "[o]ne of the most confounding problems with the opioid epidemic, from a policy perspective, is that nearly every part of the health care system has aided and abetted the spread of the epidemic in some fashion."[47]

30. The risks of opioid abuse were also discussed in publications that appeared in well-known medical journals during the period of the allegations. For example, an article by Ballantyne and Mao in the *New England Journal of Medicine* published in 2003 states:

> The follow-up should comprise regular assessment of whether the goals are being achieved, careful monitoring for signs of opioid abuse (including toxicologic screening in some cases), the use of adjunctive treatments whenever possible, and a willingness to end opioid treatment if the goals are not met.[48]
>
> Other adverse effects [of opioid therapy during prolonged treatment] include addiction and complex problems in functioning or quality of life. There are no accepted or validated risk factors for these effects, but it is widely acknowledged that there is a link between previous drug or alcohol abuse and addiction to

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[42] "CDC's Response to the Opioid Overdose Epidemic," *CDC*, available at https://www.cdc.gov/opioids/strategy.html, accessed January 21, 2019.
[43] See, for example, "Vital Signs: Overdoses of Prescription Opioid Pain Relievers—United States, 1999–2008," CDC Morbidity and Mortality Weekly Report, Volume 60, No. 43, November 4, 2011.
[44] "About AMCP," *AMCP*, available at http://www.amcp.org/AboutUs.aspx?id=8821, accessed January 21, 2019.
[45] Peter J. Neumann, "Evidence-Based and Value-Based Formulary Guidelines," *Health Affairs* 23, no. 1, 2004, pp. 124–34.
[46] "Balancing Access and Use of Opioid Therapy," AMCP Foundation Meeting Report, October 3, 2016, p. 3.
[47] "Balancing Access and Use of Opioid Therapy," AMCP Foundation Meeting Report, October 3, 2016, p. 3.
[48] Jane C. Ballantyne and Jianren Mao, "Opioid Therapy for Chronic Pain," *The New England Journal of Medicine*, 349, no. 20, 2003, pp. 1943–1953 at p. 1944.

> opioids prescribed for pain. Deterioration in functioning or quality of life appears to be closely associated with lack of motivation to improve; young adults are the most susceptible to this type of deterioration.[49]
>
> In general, noncompliance should arouse the physician's concern about possible addiction or diversion and prompt careful control and monitoring of opioid therapy. Opioid therapy should be discontinued if the behavior persists.[50]
>
> [E]vidence now suggests that prolonged, high-dose opioid therapy may be neither safe nor effective. It is therefore important that physicians make every effort to control indiscriminate prescribing, even when they are under pressure by patients to increase the dose of opioids.[51]

31. A *New York Times Magazine* 2001 article also documented diversion and street use of OxyContin.[52] It detailed personal stories of abuse in the early days of OxyContin availability in a small town in West Virginia, focusing on how quickly tolerance and dependence developed. While the article is informal and written for a general audience, it demonstrates the downsides and risks of opioids were known very early in the period of the allegations.

32. As a result of this publicly available information broadcasted by important national institutions, medical professionals, third party payors, and policy makers within Ohio had access to the information necessary to be aware of the risks of opioids and potential problems with opioid prescribing during the period of the allegations.

33. Moreover, by the Plaintiffs' own logic, such actors were and are informed regarding the risks of opioids. The Plaintiffs consider the Defendants to be informed actors because "Defendants are in the business of manufacturing, marketing, and/or distributing prescription drugs."[53] Similarly, prescribers, third party payors, and policy makers are in the business of prescribing, reimbursing, and/or legislating regarding prescription drugs. Therefore, the risks of opioids should have been "specifically known" to such prescribers, third party payors, and policy

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[49] Jane C. Ballantyne and Jianren Mao, "Opioid Therapy for Chronic Pain," *The New England Journal of Medicine*, 349, no. 20, 2003, pp. 1943–1953 at p. 1948.
[50] Jane C. Ballantyne and Jianren Mao, "Opioid Therapy for Chronic Pain," *The New England Journal of Medicine*, 349, no. 20, 2003, pp. 1943–1953 at p. 1950.
[51] Jane C. Ballantyne and Jianren Mao, "Opioid Therapy for Chronic Pain," *The New England Journal of Medicine*, 349, no. 20, 2003, pp. 1943–1953 at p. 1951.
[52] Paul Tough, "The Alchemy of OxyContin," *The New York Times Magazine*, July 29, 2001, available at https://www.nytimes.com/2001/07/29/magazine/the-alchemy-of-oxycontin.html.
[53] Complaint, ¶ 1018.

makers, particularly given that "these drugs are defined under federal and state law as substances posing a high potential for abuse and addiction."[54]

B. The Food and Drug Administration Was Aware of the Risks of Actiq and Fentora from the Time the Products Launched

34. The United States Food and Drug Administration ("FDA") is charged with, among other responsibilities, "ensuring the safety, efficacy, and security of…drugs, biological products, [and] medical devices…FDA is also responsible for advancing the public health by accelerating innovations to make medicines more effective and providing the public with accurate, science-based information on medicines…to improve their health."[55] The FDA's regulatory role begins with the approval of drugs via the New Drug Application ("NDA") process.[56] Approval by the FDA means that the agency has reviewed data on the drug and has deemed that the drug's benefits outweigh the drug's potential risks in the intended population.[57]

35. Many actions taken by the FDA, discussed next, indicate that the risks of opioid abuse are known to the FDA now, and were known to the FDA at the times of the launches of Actiq and Fentora.

36. Actiq and Fentora are both "indicated for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain."[58] The labels for Actiq and Fentora both contained black box warnings at the time of initial FDA approval. The original Actiq warning stated that "physicians and other healthcare providers must become familiar with the important warnings in this label," which included that it "**must not** be used in opioid non-tolerant patients" and that it "may be habit forming"[59]; later, the language regarding addiction was strengthened to say that "ACTIQ

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[54] Complaint, ¶ 1018.
[55] Federal Register, "Food and Drug Administration," https://www.federalregister.gov/agencies/food-and-drug-administration, accessed January 15, 2019.
[56] "New Drug Application (NDA)", *FDA*, available at https://www.fda.gov/drugs/types-applications/new-drug-application-nda, accessed January 15, 2019.
[57] "Development & Approval Process (Drugs)," *FDA*, available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/default.htm, accessed February 13, 2019.
[58] Original Actiq Label, 1998, p. 1; Original Fentora Label, 2006, p. 1.
[59] Original Actiq Label, 1998, p. 1.

exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death."[60] Fentora's 2006 label stated that it "can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing *FENTORA* in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse or diversion."[61]

37. The FDA also required Cephalon to implement certain safety programs regarding Actiq and Fentora, demonstrating knowledge of the risks of abuse of these drugs. For example, since the Food and Drug Amendments Act of 2007 ("FDAAA") took effect, the FDA has had the authority to require manufacturers to create a Risk Evaluation and Mitigation Strategy ("REMS") "to ensure that the benefits of a drug or biological product outweigh its risks."[62] According to the FDA:

> A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks…REMS are designed to help reduce the occurrence and/or severity of certain serious risks.[63]

38. REMS programs involve a "safety strategy" to achieve a specific "risk mitigation goal."[64] That safety strategy consists of either or both of two components: information to be communicated to participants in the REMS; and/or required activities to be taken by participants.[65] As examples of the former, REMS may require the drug manufacturer to provide handouts or other FDA-approved materials, either to patients "in patient-friendly language," or to healthcare professionals and their licensing entities. As examples of the latter, patients may have to register in a database or get certain tests at regular intervals; doctors might have to undergo

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[60] FDA, Actiq Label, July 2018, ("July 2018 Actiq Label"), p. 1.
[61] Original Fentora Label, 2006, p. 1.
[62] "Approved Risk Evaluation and Mitigation Strategies (REMS)," *FDA*, available at https://www.accessdata.fda.gov/scripts/cder/rems/, accessed February 16, 2019.
[63] "Risk Evaluation and Mitigation Strategies (REMS)," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/default.htm, accessed January 8, 2019.
[64] What's in a REMS?" *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592636.htm, accessed January 8, 2019.
[65] "What's in a REMS?" *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592636.htm, accessed January 8, 2019.

training or "agree to counsel their patients about the particular risk"; or the drug might have to be dispensed by a hospital or other healthcare facility, rather than a retail pharmacy.[66]

39. In determining whether a REMS is necessary, the FDA may seek out information from outside experts, patients, healthcare providers or an FDA Advisory Committee.[67] Manufacturers are then notified about the need to implement a REMS, who in turn submit a proposal for FDA approval; once approved it is the responsibility of the drug manufacturer to carry out the requirements outlined in a REMS.[68]

40. The FDA states that "[m]edications with a REMS would not be approved or would be withdrawn from the market without the REMS in place."[69] The FDA may require a REMS for a drug prior to approval, or may decide a REMS is necessary for an already approved drug. For example, Entereg was required to have a REMS as part of the drug approval process before it was approved in May of 2008.[70] Conversely, Androgel 1%, which was approved in February of 2000,[71] had a REMS approved in September of 2009, nearly a decade after the drug's initial approval.[72]

41. Prior to the passage of the FDAAA, the FDA occasionally used similar programs, called Risk Minimization Action Plans ("RiskMAPs"), to achieve similar aims. As defined in a 2005 FDA report on risk minimization, a RiskMAP is "a strategic safety program designed to meet specific goals and objectives in minimizing known risks of a product while preserving its benefits. A RiskMAP targets one or more safety-related health outcomes or goals and uses one

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[66] "What's in a REMS?" *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592636.htm, accessed January 8, 2019, at pp. 2–3.
[67] "Roles of Different Participants in REMS," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592662.htm, accessed January 8, 2019.
[68] "Roles of Different Participants in REMS," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592662.htm, accessed January 8, 2019.
[69] "Roles of Different Participants in REMS," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/REMS/ucm592662.htm, accessed January 8, 2019.
[70] Letter from Julie Beitz (Center for Drug Evaluation and Research) to Linda G. Young (Adolor Corporation), "NDA 21-775" May 20, 2008, pp. 1, 3–4, 6.
[71] "Drugs@FDA: FDA Approved Drug Products," *FDA*, available at https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&AppINo=021015, accessed January 8, 2019.
[72] "Approved Risk Evaluation and Mitigation Strategies (REMS)–Androgel 1% (testosterone)," *FDA*, available at https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=4, accessed January 8, 2019.

or more tools to achieve those goals."[73] The suggested tools are similar to REMS tools, including "documentation of safe-use conditions" such as lab test results, "compulsory reminder systems," and prescribing or dispensing only by certified prescribers or dispensers.[74]

42. Prior to 2011, Actiq and Fentora were covered by these earlier risk mitigation plans. Actiq was approved with a restricted distribution program to prevent exposure to children and potential abuse.[75] In September of 2006, the package insert for Actiq was converted to a medication guide, which informs patients about the risks associated with the drug—including physical dependence, abuse, and addiction[76]—and is required to be given to patients when the prescription is filled.[77] When Fentora was approved it also required a medication guide.[78] In July of 2009, the FDA decided that a separate REMS for each Transmucosal Immediate-Release Fentanyl ("TIRF") product would be too burdensome on the healthcare system, and began a discussion of a single-shared REMS for all TIRF products.[79] This led to the TIRF REMS program as discussed above.

43. Since 2012, both Actiq and Fentora have been included in a mandatory REMS covering TIRF products; that REMS was updated most recently in 2017.[80] The TIRF REMS has the goal of mitigating "risk of misuse, abuse, addiction, overdose and serious complications due to

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[73] CDER and CBER, "Guidance for Industry: Development and Use of Risk Minimization Action Plans," FDA Report, March 2005, p. 5.
[74] CDER and CBER, "Guidance for Industry: Development and Use of Risk Minimization Action Plans," FDA Report, March 2005, p. 10.
[75] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, p. 2. I note that Plaintiffs' expert Dr. David Kessler stated Actiq "would not have been approved but for" the risk management program. Deposition of Dr. David Kessler, April 25–26, 2019, pp. 668:11–15.
[76] Original Actiq Label, p. 53.
[77] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, p. 3.
[78] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, p. 3.
[79] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, p. 5.
[80] "Approved Risk Evaluation and Mitigation Strategies (REMS)–Transmucosal Immediate-Release Fentanyl (TIRF) Products," *FDA*, available at https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=60, accessed January 8, 2019; "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf.

medication errors."[81] The TIRF REMS consists of several elements. These include, among others, requirements on various agents in the healthcare system:

- "Healthcare providers who prescribe TIRF medicines for outpatient use must review the prescriber educational materials, enroll in the REMS program, and commit to comply with the REMS requirements."[82] The prescriber educational materials cover the definition of opioid tolerance, contraindications, risk of abuse and addiction, possible measures to mitigate such risk, and others.[83]
- "Patients…must…sign a Patient-Prescriber Agreement Form."[84]
- "Pharmacies [both inpatient and outpatient]...must enroll in the program [and] train their pharmacy staff on the REMS requirements."[85]
- "Wholesalers and distributors…must enroll in the program and commit to distributing only to authorized enrolled pharmacies."[86]

44. REMS programs have been applied to other opioids as well. In July of 2012, the FDA placed all extended-release, long-acting opioids into a single REMS.[87] Opioids such as OxyContin, Kadian, and Nucynta ER, as well as their generics were included in the REMS.[88] The REMS had the goal of reducing "serious adverse outcomes resulting from inappropriate

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[81] "Transmucosal Immediate Release Fentanyl (TIRF) Products Risk Evaluation and Mitigation Strategy (REMS): Education Program for Prescribers and Pharmacists," TIRF REMS Access Manual, undated, available at https://www.tirfremsaccess.com/TirfUI/rems/pdf/education-and-ka.pdf, p. 2.
[82] "Frequently Asked Questions," TIRF REMS Access Manual, undated, available at https://www.tirfremsaccess.com/TirfUI/rems/pdf/faq.pdf, p. 2.
[83] "Transmucosal Immediate Release Fentanyl (TIRF) Products Risk Evaluation and Mitigation Strategy (REMS): Education Program for Prescribers and Pharmacists," TIRF REMS Access Manual, undated, available at https://www.tirfremsaccess.com/TirfUI/rems/pdf/education-and-ka.pdf.
[84] "Frequently Asked Questions," TIRF REMS Access Manual, undated, available at https://www.tirfremsaccess.com/TirfUI/rems/pdf/faq.pdf, p. 2.
[85] "Frequently Asked Questions," TIRF REMS Access Manual, undated, available at https://www.tirfremsaccess.com/TirfUI/rems/pdf/faq.pdf, pp. 2–3.
[86] "Frequently Asked Questions," TIRF REMS Access Manual, undated, available at https://www.tirfremsaccess.com/TirfUI/rems/pdf/faq.pdf.
[87] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, pp. 8, 22. This REMS has since been deprecated in favor of a new one, which I discuss below.
[88] "List of Extended-Release and Long-Acting Opioid Products Required to Have an Opioid REMS," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm251735.htm, accessed February 15, 2019.

prescribing, misuse, and abuse of extended-release or long-acting (ER/LA) opioid analgesics while maintaining patient access to pain medications."[89] The REMS consisted of the following elements:

- "A Medication Guide will be dispensed with each ER/LA opioid analgesic prescription."[90]
- "Training will be made available to healthcare providers who prescribe ER/LA opioid analgesics."[91] This training was voluntary.[92]

45. In 2018, the FDA approved a broader REMS covering both long-acting opioids as well as immediate-release opioids not already covered by another REMS (such as the TIRF REMS).[93] This REMS covers drugs like hydrocodone-acetaminophen combinations, oxycodone, and oxycodone-acetaminophen combinations.[94] This REMS requires opioid analgesic companies to provide education to healthcare providers, including prescribers and those who participate in the treatment and monitoring of patients, and "information for [providers] to use when counseling patients about the risks of ER, LA, and IR opioid analgesic use."[95] However, I note that these programs are voluntary, and per the FDA, "[t]here is no mandatory federal requirement that prescribers or other [healthcare providers] take the training and no precondition to prescribing or

[89] "Extended-Release (ER) and Long-Acting (LA) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS)," FDA REMS, Paperwork Reference ID 3784602, June 26, 2015, p. 2.
[90] "Extended-Release (ER) and Long-Acting (LA) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS)," FDA REMS, Paperwork Reference ID 3784602, June 26, 2015, at p. 2.
[91] "Extended-Release (ER) and Long-Acting (LA) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS)," FDA REMS, Paperwork Reference ID 3784602, June 26, 2015, at p. 2.
[92] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, p. 22.
[93] "Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm, accessed February 15, 2019; "FDA Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain," *FDA*, September 2018, available at https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_analgesic_2018_09_18_FDA_Blueprint.pdf.
[94] "Approved Risk Evaluation and Mitigation Strategies (REMS)–Opioid Analgesic REMS," *FDA*, available at https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=17, accessed February 15, 2019.
[95] "FDA Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain," *FDA*, September 2018, available at https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_analgesic_2018_09_18_FDA_Blueprint.pdf, p. 1.

dispensing opioid analgesics to patients."[96] The FDA states that it "continues to consider whether there are circumstances when the FDA should require some form of mandatory education."[97]

46. In sum, through labeling and the requirements of the risk management programs, the FDA provided information to physicians and patients about the risks associated with opioid products throughout the period of the allegations.

47. In fact, the FDA has not rescinded approval or substantially changed the label of Actiq or Fentora. Additionally the FDA has approved several new TIRF products (and thus subject to the joint TIRF REMS) since it approved Actiq and Fentora.[98] All these factors indicate that despite the known risks, the FDA considered the benefits of TIRF products such as Actiq and Fentora sufficiently high to exceed such risks.

48. The FDA itself has even recognized that it should have more rigorously and proactively used its tools to mitigate problems of opioid overutilization and abuse. In February of 2019, then Commissioner of the FDA, Dr. Scott Gottlieb released a statement noting that "the scope of the [opioid] epidemic reflects many past mistakes and many parties who missed opportunities to stem the crisis, including the FDA."[99] He went on to list some of the areas in which the FDA was planning on taking action in the upcoming year including changes to packaging to reduce opioid abuse, increasing access to addiction recovery tools such as over-the-counter ("OTC") naloxone, strengthening commitment to "non-addictive" pain treatments, and stanching the flow of illicit opioids.[100] Specifically in reference to the TIRF REMS, Dr. Gottlieb mentioned the FDA "has been actively assessing the recommendations of our advisory committee on the

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[96] "Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm, accessed February 15, 2019.
[97] "Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)," *FDA*, available at https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm, accessed February 15, 2019.
[98] "Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse," *FDA*, available at https://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM566985.pdf, pp. 5–7; "Approved Risk Evaluation and Mitigation Strategies (REMS)," *FDA*, available at https://www.accessdata.fda.gov/scripts/cder/rems/, accessed February 16, 2019, pp. 1–2.
[99] FDA Press Release, "Statement from FDA Commissioner Scott Gottlieb, M.D. on the Agency's 2019 Policy and Regulatory Agenda for Continued Action to Forcefully Address the Tragic Epidemic of Opioid Abuse," February 26, 2019.
[100] FDA Press Release, "Statement from FDA Commissioner Scott Gottlieb, M.D. on the Agency's 2019 Policy and Regulatory Agenda for Continued Action to Forcefully Address the Tragic Epidemic of Opioid Abuse," February 26, 2019.

effectiveness of the REMS and necessary changes. Based on these recommendations, and our analysis of our own data, the FDA will soon share next steps, including modifications intended to strengthen the current TIRF REMS."[101]

C. Since its Inception, the Drug and Enforcement Administration Was Aware of the Risks of Opioids

49. The Drug Enforcement Administration ("DEA"), a part of the U.S. Department of Justice ("DOJ"), is charged with enforcing the controlled substances laws and regulations of the U.S.[102] The DEA has many responsibilities related to this mission, including the "[m]anagement of a national drug intelligence program…to collect, analyze, and disseminate strategic and operational drug intelligence information" and the "[e]nforcement of the provisions of the Controlled Substances Act as they pertain to the manufacture, distribution, and dispensing of legally produced controlled substances."[103]

50. Under authority of the Controlled Substances Act established in 1970, the DEA determines "drug scheduling," which determines whether, and under what federal government restrictions, the drugs may be legally sold, distributed, and used in the U.S.[104] There are five "schedules."[105] Schedule I drugs are not approved for any medical uses and include substances like heroin and MDMA (ecstasy).[106] Schedules II–V include drugs that have approved medical uses, with Schedule II containing the substances with the highest potential for abuse, and Schedule V containing the substances with the lowest potential for abuse.[107] Most opioids are part of Schedule II, except for certain low-dose products like cough preparations.[108] Actiq and

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[101] FDA Press Release, "Statement from FDA Commissioner Scott Gottlieb, M.D. on the Agency's 2019 Policy and Regulatory Agenda for Continued Action to Forcefully Address the Tragic Epidemic of Opioid Abuse," February 26, 2019.
[102] "Drug Enforcement Administration," *DEA*, available at https://www.federalregister.gov/agencies/drug-enforcement-administration, accessed January 15, 2019.
[103] "Mission," *DEA*, available at https://www.dea.gov/mission, accessed February 15, 2019.
[104] "Drug Scheduling," *DEA*, available at https://www.dea.gov/drug-scheduling, accessed January 15, 2019.
[105] "Drug Scheduling," *DEA*, available at https://www.dea.gov/drug-scheduling, accessed January 15, 2019.
[106] "Drug Scheduling," *DEA*, available at https://www.dea.gov/drug-scheduling, accessed January 15, 2019.
[107] "Drug Scheduling," *DEA*, available at https://www.dea.gov/drug-scheduling, accessed January 15, 2019.
[108] "Drug Scheduling," *DEA*, available at https://www.dea.gov/drug-scheduling, accessed January 15, 2019; "Schedules of Controlled Substances," *Federal Register* 36, no. 80, April 24, 1971, pp. 7802–7812 at p. 7804.

other fentanyl products, including Fentora, are Schedule II drugs, indicating a high potential for abuse.[109]

51. The DEA does not permit refills on Schedule II prescriptions,[110] and state regulators may further set time expiration windows for Schedule II prescriptions.[111] Further, under Schedule II, pharmacists may dispense emergency medications, but only if "[t]he quantity prescribed and dispensed is limited to the amount adequate to treat the patient during the emergency period."[112] Despite these known risks, the DEA permits the promotion, distribution, sale and use of opioid products because they have "a currently accepted medical use in treatment in the United States."[113]

52. The opioids at issue here have been scheduled aggressively since nearly the inception of the Controlled Substances Act. As early as April 24, 1971 fentanyl, oxycodone and hydrocodone were all listed as Schedule II drugs.[114] This scheduling indicates that the DEA was aware of the risks of drugs like Actiq, Fentora, and OxyContin decades before these drugs were approved for sale in the U.S.

D. Evidence Indicates that Many Physicians Prescribed Opioid Products Despite Knowing that They Were Being Used for Non-Medical Purposes

53. Evidence suggests that physicians were aware of the risks of opioids. As discussed above, there were many instances of federal regulators, academic institutions, and medical groups disseminating and discussing information about the risks of opioids. In addition there is a plethora of evidence available to show that many patients do not use opioid painkillers for legitimate medical purposes. See Section IV.A. Despite this evidence, many physicians continue to prescribe opioids to these patients.

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[109] Original Actiq Label, 1998, p. 22.
[110] "Section V – Valid Prescription Requirements," *DEA*, available at https://www.deadiversion.usdoj.gov/pubs/manuals/pract/section5.htm, accessed February 15, 2019.
[111] "4 Controlled Substance Laws and Regulations You Should Know," *Pharmacy Times*, available at https://www.pharmacytimes.com/contributor/jennifer-gershman-pharmd-cph/2017/07/4-controlled-substance-laws-and-regulations-you-should-know-, accessed February 15, 2019.
[112] "Part 1306 – Prescriptions: Controlled Substances Listed in Schedule II," *DEA*, available at https://www.deadiversion.usdoj.gov/21cfr/cfr/1306/1306_11.htm, accessed February 15, 2019.
[113] "Subchapter 1 – Control and Enforcement: Part B – Authority to Control; Standards and Schedules," *DEA*, available at https://www.deadiversion.usdoj.gov/21cfr/21usc/812.htm, accessed May 8, 2019.
[114] "Schedules of Controlled Substances," *Federal Register* 36, no. 80, April 24, 1971, pp. 7802–7812 at p. 7804.

54. For example, some doctors have established "pill mills" to prescribe and dispense a large number of opioids. A "pill mill" is a "doctor, clinic, or pharmacy that is prescribing or dispensing powerful narcotics inappropriately or for non-medical reasons."[115] A pill mill is a concrete example of doctors knowingly dispensing opioids for non-medical purposes.

55. As noted in an investigative report, Ohio is or was home to several pill mills.[116] In particular, the Bellwether Counties contained such pill mills. For example, a doctor based in Akron was alleged by Federal Prosecutors to have distributed thousands of painkillers from his office between August 2011 and October 2012.[117] Similarly, authorities in Cuyahoga County charged Dr. Ronald Celeste with operating a pill mill, alleging he wrote over thirty thousand prescriptions "in large amounts and in dangerous combinations."[118] "The pills went from doctors [sic] offices straight to the streets, translating into addiction for many residents – and a business for many doctors."[119]

56. Evidence suggests that doctors acting in such a manner may have contributed to issues with opioid abuse. A qualitative study funded by the National Institute on Drug Abuse conducted in 2010 found evidence to suggest "that the prescription medications being dispensed in record number by pain clinics are prominent among the drugs identified in a majority of overdose deaths. This also suggests that a significant proportion of the pills prescribed from these facilities may be ending up in the hands of abusers and/or traffickers."[120] Some participants in the study (actual drug users who frequented the pill mills) compared the practice to illicit drug

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[115] Pia Malbran, "What's a Pill Mill?" *CBS News*, June 5, 2007, available at https://www.cbsnews.com/news/whats-a-pill-mill/, accessed February 25, 2019.
[116] Ron Regan et al., "How State Regulators Allowed Ohio's Pill Mill Crisis to Explode," News 5 Cleveland, October 30, 2018, available at https://www.news5cleveland.com/longform/how-state-regulators-allowed-ohios-pill-mill-crisis-to-explode, accessed May 2, 2019.
[117] Ron Regan et al., "How State Regulators Allowed Ohio's Pill Mill Crisis to Explode," News 5 Cleveland, October 30, 2018, available at https://www.news5cleveland.com/longform/how-state-regulators-allowed-ohios-pill-mill-crisis-to-explode, accessed May 2, 2019.
[118] Kara Sutyak, "Doctor Accused of Running Pill Mill," December 19, 2013, available at https://fox8.com/2013/12/19/doctor-accused-of-running-pill-mill/.
[119] Ron Regan et al., "How State Regulators Allowed Ohio's Pill Mill Crisis to Explode," News 5 Cleveland, October 30, 2018, available at https://www.news5cleveland.com/longform/how-state-regulators-allowed-ohios-pill-mill-crisis-to-explode, accessed May 2, 2019.
[120] Khary K. Rigg et al., "Prescription Drug Abuse & Diversion: Role of the Pain Clinic," *Journal of Drug Issues* 40, no. 3, 2010, pp. 681–702 at p. 684.

dealing, with one interviewee stating "[t]hey are cash only businesses like selling drugs on the street, except they've got an office for it."[121]

57. Hence, because some physicians prescribed opioid products despite knowing that they were being used for non-medical purposes, these physicians could not have been misled by the Teva Defendants' alleged false marketing messages, but were rather induced by personal financial gain to write an exorbitant number of opioid prescriptions.

E. During the Period of the Allegations, Ohio Medicaid, Medicare and Private Payors Were Aware, or Should Have Been Aware of Issues Relating to Opioid Abuse in the State of Ohio

58. As will be discussed in Section V.A, the majority of opioid products are reimbursed for by third party payors ("TPPs"). Thus, the coverage and reimbursement policies of these payors are relevant because such policies affected the number of prescriptions of opioids, and in particular the prescriptions of opioid products sold by the Teva and Actavis Generic Defendants.

59. Most private health insurance plans, either obtained through an employer or as an individual, have a prescription drug benefit.[122] However, the private health insurance company or the employer typically does not administer the prescription drug coverage.[123] Instead, pharmacy benefit managers ("PBMs") handle most aspects of the benefit, other than the actual monetary risk. In particular, PBMs provide "administrative services" ("client service, pharmacy network administration, mail pharmacy, claims adjudication, member services, and manufacturer contracting and rebate administration") and "clinical services," which "range from formulary

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[121] Khary K. Rigg et al., "Prescription Drug Abuse & Diversion: Role of the Pain Clinic," *Journal of Drug Issues* 40, no. 3, 2010, pp. 681–702 at p. 687.

[122] "What Marketplace Health Insurance Plans Cover," *HealthCare.gov*, available at https://www.healthcare.gov/coverage/what-marketplace-plans-cover/, accessed January 8, 2019; "2017 Employer Health Benefits Survey, Section 9: Prescription Drug Benefits," Kaiser Family Foundation, September 19, 2017, available at https://www.kff.org/report-section/ehbs-2017-section-9-prescription-drug-benefits/, accessed January 8, 2019, p. 197.

[123] "Study of Pharmaceutical Benefit Management," Pricewaterhouse Coopers HCFA Contract No. 500-97-0399/0097, June 2001 ("Study of Pharmaceutical Benefit Management"), p. 5. This study provides an excellent summary of the PBM industry at the time it was written, near the beginning of the period at issue. A more current summary can be found in Robert P. Navarro et al., "Chapter 11: Prescription Drug Benefits in Managed Care," in *Essentials of Managed Health Care*, Sixth Edition, ed. Peter R. Kongstvedt (Burlington, MA: Jones and Bartlett Learning, 2013) ("Prescription Drug Benefits in Managed Care"), pp. 259–260.

management to sophisticated disease management programs."[124] PBMs are therefore responsible for many decisions regarding private prescription drug insurance reimbursement.

60. PBMs are frequently contracted by health insurers due to their abilities to lower costs. The three primary ways they achieve such savings are through elevated efficiency in administration; negotiating for discounts and rebates with pharmacies and drug manufacturers; and "managing drug utilization" by "using clinical services that influence the behavior of the physicians, pharmacist, and patient."[125] PBMs have an array of tools that achieve this utilization management and which, therefore, have been used to influence opioid prescriptions, and as will be explained below in Section V, could have been used even further.

61. It is important to note that PBMs have Pharmacy and Therapeutics ("P&T") committees that play a large role in deciding coverage policies. P&T committees are informed entities, and they have an incentive to remain informed.[126] A P&T committee is typically "comprised of physicians, pharmacists, and other clinicians" and must meet regularly due to the fast pace of pharmaceutical innovation.[127] This is important because, as discussed next, P&T committees would have known, or should have obtained, information about the risks of opioids (including the Teva and Actavis Generic Defendants' opioid products) during the period of the allegations.

62. The American Society of Health-System Pharmacists,[128] in its "Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System" (the "Guidelines"), confirms that the priority in benefit design should be patient health,[129] and that design should be based on appropriate evidence:

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[124] Study of Pharmaceutical Benefit Management, at p. 17.
[125] Study of Pharmaceutical Benefit Management, at p. 5.
[126] Study of Pharmaceutical Benefit Management, at p. 79.
[127] Study of Pharmaceutical Benefit Management, at p. 79.
[128] This organization is officially interested in formulary design for health systems, such as hospitals and doctor groups, rather than managed care organizations. However, the Academy of Managed Care Pharmacy is primarily focused on managed care formularies, and in its publication of *The AMCP Format for Formulary Submissions, Version 4.0*, it cites these guidelines as an approach to decision making, given the properly formatted formulary submission. See "The AMCP *Format* for Formulary Submissions, Version 4.0: A Format for Submission of Clinical and Economic Evidence in Support of Formulary Consideration," Academy of Managed Care Pharmacy, available at http://www.amcp.org/FormatV4/, April 2016.
[129] Linda S. Tyler et al., "ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System," *American Journal of Health-System Pharmacists* 65, 2008 ("ASHP Guidelines"), pp. 166–175 at p. 167.

> Inclusion of a medication on a health system's formulary should reflect than evidence-based evaluation of the relative merits and risks of the medication has been performed and that the institutions P&T committee, with input from appropriate experts, has determined that the medication is appropriate…Evidence-based medicine is a systematic approach to the evaluation of biomedical literature and application to clinical practice…[P]ractitioners must be proficient in retrieving, evaluating, and applying the biomedical literature to clinical practice.[130]

63. The Guidelines specifically discuss two situations pertinent to this matter. The first is off-label use: "When the off-label use of an agent is expected to occur frequently, the P&T committee should establish protocols guiding that use."[131] Second, "[t]he use of high-risk medications…offer[s an] opportunit[y] to perform proactive risk assessments."[132]

64. Other sources document that P&T committees are informed bodies. For example, the University of Wisconsin-Madison Division of Pharmacy Professional Development lists, among its "5 Best Practices for P&T Committee Members," the need for committee members to "be informed," "be objective," and "emphasize patient-focused outcomes."[133] In particular, to stay informed, "[t]hey should regularly seek out information from reputable sources, including peer-reviewed journals, industry thought-leaders and the FDA." With respect to being objective, the Division notes that "[f]ormulary decisions are objective and evidence-based." Finally, when discussing the focus on patient outcomes, P&T committee members "should be focused on the quality, efficacy, and safety of the treatment patients receive."[134]

65. Given this responsibility to stay informed, prudent P&T committee members would have been aware of the nationally available information and voicing of concern about the risks of opioids discussed above.

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[130] ASHP Guidelines, p. 168.
[131] ASHP Guidelines, p. 171.
[132] ASHP Guidelines, p. 172.
[133] UW-Madison School of Pharmacy, Division of Pharmacy Professional Development, "5 Best Practices for P&T Committee Members," available at https://ce.pharmacy.wisc.edu/blog/5-best-practices-for-pt-committee-members/.
[134] "5 Best Practices for P&T Committee Members," *UW-Madison School of Pharmacy, Division of Pharmacy Professional Development*, available at https://ce.pharmacy.wisc.edu/blog/5-best-practices-for-pt-committee-members/, accessed January 10, 2019.

66. In fact, Plaintiffs use PBMs and other agents to administer their employee health care plans.[135] Notably, despite filing this lawsuit, Plaintiffs and their PBMs still cover prescription opioids to treat chronic pain for their plan members.[136] As Cuyahoga County has made clear, "[w]e've always covered them. There would have been no change just because of the litigation."[137]

V. Plaintiffs and Plaintiffs' Experts Do Not Appropriately Consider the Role that Third Party Payors Play in Physicians' Prescribing of Opioid Drugs, as Well as Third Party Payors' Financial Incentives to Encourage Opioid Prescribing

A. Third Party Payors—Including Medicaid, Medicare, and Private Insurers—Reimburse for the Majority of the Teva and Actavis Generic Defendants' Opioid Prescriptions

67. There are many ways an individual can obtain health insurance. These include Medicaid, Medicare, private insurance through an employer, individually purchased private insurance, and insurance obtained through the military.

68. The Ohio Medicaid program is funded by the federal government and by the State of Ohio and covers several groups of Ohio residents, including low-income individuals, pregnant women, and individuals with disabilities.[138] Most Ohio Medicaid beneficiaries receive healthcare from a managed care plan, which is a private health insurance plan that "provide[s] comprehensive healthcare services to members" and "offer[s] financial incentives for patients to

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[135] Deposition of Margaret June Carr, December 21, 2018 ("Carr Deposition"), p. 44:21–24 ("Q. You -- you said that Express Scripts was the PBM that worked on the county's medical health plan for a long time, correct? A. Correct."); Deposition of Holly Woods, January 7, 2019 ("Woods Deposition"), p. 25:18–25. ("Q. The County contracts with PBMs such as CVS Caremark to administer the prescription drug plan, right? A. Correct.").

[136] Woods Deposition, p. 22:9–15 ("Q. I'll try. Does the County pay for prescription opioids for the treatment of chronic pain for county employees, court employees, and potentially former employees being covered under worker's compensation? A. The County does pay through our pharmacy benefit manager."); Woods Deposition, p. 38:12–15 ("Q. … [T]he county continues to cover prescription opioids through its healthcare plan today, right? A. Yes."); Woods Deposition, p. 43:6–9 ("Q. Is there any reason that the County decided to continue covering prescription opioids under its healthcare plan even after filing this lawsuit? … A. We follow best practices."); Carr Deposition, p. 156:13–21 ("Q. Is there a reason that the county decided to continue covering prescription opioids under its employee health plan after filing the lawsuit? A… We've always covered them. There would have been no change just because of the litigation.").

[137] *Id.*

[138] "Who Qualifies for Coverage?" *Ohio Department of Medicaid*, available at https://medicaid.ohio.gov/FOR-OHIOANS/Who-Qualifies, accessed May 2, 2019.

use the providers who belong to the plan."[139] These plans hold provider agreements with the Ohio Department of Medicaid ("ODM") to provide coordinated healthcare services to Medicaid beneficiaries.[140]

69. In addition to Medicaid and private insurance, Medicare is an important TPP, primarily insuring patients age 65 and older, administered by the Centers for Medicare & Medicaid Services ("CMS"), and paid for mostly by the federal government.[141]

70. **Exhibit 3** shows the shares of Ohio residents that obtain health insurance coverage from different sources. The exhibit shows that, in general, the vast majority of individuals in Ohio have health insurance. Over time, there has been an increase in the fraction covered by government payors, a decrease in those covered by employment based insurance, and a decrease in the fraction of uninsured.

71. Similar trends in coverage can be seen for prescription drugs in general, and opioids in particular: A large and increasing share of opioid prescriptions in the U.S. are paid for by third party payors. Zhou and coauthors found that in 2012, 9 percent of opioid costs were covered by Medicaid, 26 percent by Medicare, 18 percent by out-of-pocket payments and most of the balance by private insurance.[142] In contrast, in 1999, Medicaid and Medicare only covered 9 percent of costs, while 53 percent of costs were borne out-of-pocket. A study of Rhode Island's prescription drug monitoring program records from 2015 showed that 51 percent of opioid prescriptions were covered by private insurance, 29 percent were covered by Medicare, 8 percent were covered by Medicaid, 9 percent were covered out-of-pocket, and the remainder were covered by other federal sources like the U.S. Department of Veterans Affairs.[143] Thus, TPPs reimburse for the majority of opioid prescriptions today and have accounted for a substantial

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[139] "Managed Care," *Ohio Department of Medicaid*, available at https://medicaid.ohio.gov/FOR-OHIOANS/Programs#623507-managed-care, accessed May 2, 2019; "Medicaid Managed Care FAQ," *Ohio Department of Medicaid*, available at https://www.ohiomh.com/resources/medicaidfaq, accessed May 2, 2019.
[140] "Managed Care," *Ohio Department of Medicaid*, available at https://medicaid.ohio.gov/FOR-OHIOANS/Programs#623507-managed-care, accessed May 2, 2019.
[141] Prescription Drug Benefits in Managed Care, p. 273; "How is Medicare Funded?" *Medicare.gov*, available at https://www.medicare.gov/about-us/how-is-medicare-funded, accessed February 15, 2019.
[142] Chao Zhou et al., "Payments for Opioids Shifted Substantially to Public and Private Insurers While Consumer Spending Declined, 1999–2012," *Health Affairs* 35, no. 5, 2018, pp. 824–831.
[143] Hilary Aroke et al., "Estimating the Direct Costs of Outpatient Opioid Prescriptions: A Retrospective Analysis of Data from the Rhode Island Prescription Drug Monitoring Program," *Journal of Managed Care & Specialty Pharmacy* 24, no. 3, 2018, pp. 214–224.

portion of spending as far back as 1999. Understanding how TPPs' policies affect opioid prescriptions is therefore important for understanding the causes of the trends in opioid utilization—and any allegedly medically unnecessary opioid prescriptions—over time.

72. While I could not locate similar data on payor breakdown for the Teva and Actavis Generic Defendants' opioid products in particular, internal marketing documents show that Fentora was paid for 80 percent of the time by commercial insurance, 14 percent of the time by Medicare, and 1 percent of the time with cash, with the remaining 5 percent unlabeled.[144] This suggests that the Teva and Actavis Generic Defendants' opioid products are usually paid for by third party payors, just as with healthcare more generally.

73. Next, I consider the role that these TPPs have in influencing opioid prescriptions. As I discussed earlier in this report, the risks of opioid abuse have been known throughout the period of the allegations, and TPPs could have implemented tools to limit opioid prescriptions.

B. Ohio Medicaid, Medicare and Private Payors Did Not Use Available Tools to Limit Opioid Prescriptions, Including Prescriptions for the Teva and Actavis Generic Defendants' Drugs

74. Ohio Medicaid, Medicare, and private payors have a number of tools that can influence the prescribing behavior of physicians and the use of prescription drugs, including opioid drugs. Despite having knowledge of the risks of opioids during the period of the allegations, TPPs failed to adequately use these tools.

75. By way of example, Ohio Medicaid beneficiaries can obtain prescription drug coverage in several ways. As discussed earlier, most Ohio Medicaid beneficiaries receive health care from a managed care plan, which is a private health insurance plan that "provide[s] comprehensive healthcare services to members" and "offer[s] financial incentives for patients to use the providers who belong to the plan."[145] Ohio Medicaid offers five options for managed care plans: Buckeye Health Plan, CareSource, Molina Healthcare, Paramount Advantage, and United

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[144] Teva Presentation, "US Specialty Medicines: CNS Fentora 2014 Annual Operating Plan," August 2013, TEVA_MDL_A_00763899 at slide 24.

[145] "Managed Care," *Ohio Department of Medicaid*, https://medicaid.ohio.gov/FOR-OHIOANS/Programs#623507-managed-care, accessed May 2, 2019; "Medicaid Managed Care FAQ," *Ohio Department of Medicaid*, available at https://www.ohiomh.com/resources/medicaidfaq, accessed May 2, 2019; "Definitions of Health Insurance Terms," *Bureau of Labor Services*, available at https://www.bls.gov/ncs/ebs/sp/healthterms.pdf.

Healthcare.[146] Individuals have the choice of electing which of these managed care plans to enroll in; if no plan is selected, Ohio Medicaid will assign the beneficiaries to one of these plans.[147] In addition, Ohio Medicaid also offers fee-for-service healthcare through a network of providers.[148] Providers in this fee-for-service network bill Medicaid directly for any services provided to Medicaid beneficiaries.[149]

76. Though Ohio Medicaid beneficiaries can obtain coverage for prescription drugs in several different ways, tools similar to those available to private plans can be used to influence the prescription drug utilization of beneficiaries. As of October 1, 2011, prescription drug coverage for Ohio Medicaid beneficiaries has been managed by managed care plans for MCP enrollees.[150] All five managed care plans are administered by PBMs, just as many private plans are, as discussed above.[151] Ohio Medicaid's fee-for-service prescription drug benefit, the Ohio Medicaid Drug program, is administered by the Ohio Department of Medicaid ("ODM").[152] According to the ODM, it aims to use its drug coverage policies "to ensure the effective use of healthcare by improving patient access to affordable care, minimizing overall medical costs and improving the quality of life for…[Medicaid] recipients."[153]

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[146] "Choosing a Managed Care Plan," *Ohio Department of Medicaid*, available at https://medicaid.ohio.gov/FOR-OHIOANS/Programs/Managed-Care-for-Ohioans, accessed May 2, 2019.
[147] "Choosing a Managed Care Plan," *Ohio Department of Medicaid*, available at https://medicaid.ohio.gov/FOR-OHIOANS/Programs/Managed-Care-for-Ohioans, accessed May 2, 2019; "Medicaid Managed Care FAQ," *Ohio Department of Medicaid*, available at https://www.ohiomh.com/resources/medicaidfaq, accessed May 2, 2019.
[148] "Getting Care," *Ohio Department of Medicaid*, available at https://www.medicaid.ohio.gov/FOR-OHIOANS/Already-Covered/Getting-Care, accessed May 2, 2019.
[149] "Getting Care," *Ohio Department of Medicaid*, available at https://www.medicaid.ohio.gov/FOR-OHIOANS/Already-Covered/Getting-Care, accessed May 2, 2019.
[150] "Welcome to the Ohio Medicaid Pharmacy Program," *Ohio Department of Medicaid*, available at https://pharmacy.medicaid.ohio.gov/, accessed May 3, 2019.
[151] "Comprehensive Preferred Drug List," Buckeye Health Plan Report, April 1, 2019, p. 6, available at https://www.buckeyehealthplan.com/content/dam/centene/envolve-pharmacy-solutions/pdfs/PDL/FORMULARY-BuckeyeHealthPlan_Ohio.pdf; *CareSource.com*, available at https://www.caresource.com/oh/providers/education/patient-care/pharmacy/medicaid/; "Drug Formulary," *Molina*, available at https://www.molinahealthcare.com/providers/fl/medicaid/drug/pages/formulary.aspx; "Prescription," *Paramount*, available at https://www.paramounthealthcare.com/services/brokers/plans-and-services/prescription; "Pharmacy," *UnitedHealthcare*, available at https://www.uhc.com/employer/pharmacy; Ohio Auditor of State Press Release, "Auditor's Report: Pharmacy Benefit Managers Take Fees of 31% on Generic Drugs Worth $280M in One-Year Period," August 16, 2018.
[152] "Ohio Medicaid Pharmacy Reference Guide," *Ohio Department of Medicaid*, April 2018, available at https://pharmacy.medicaid.ohio.gov/sites/default/files/2018-04-30-mcp-and-mycare-pharmacy-reference-guide.pdf; "Welcome to the Ohio Medicaid Pharmacy Program," *Ohio Department of Medicaid*, available at https://pharmacy.medicaid.ohio.gov/, accessed May 3, 2019.
[153] "Drug Coverage Information," *Ohio Department of Medicaid*, 2018, available at https://pharmacy.medicaid.ohio.gov/drug-coverage.

77. Medicare beneficiaries can obtain prescription drug benefits in two ways. First, they can enroll in a Medicare Part D plan—a stand-alone plan that covers prescription drugs.[154] Second, they can choose to enroll in a Medicare Advantage plan—"an 'all in one' alternative to Original Medicare…offered by private companies approved by Medicare."[155]

78. While Medicare Part D and Medicare Advantage are primarily funded by the federal government, they are administered by private health insurance companies, in much the same way that private health insurance is administered.[156] These private health insurance companies often use PBMs to administer Medicare plans, just like PBMs are used for administering commercial insurance plans and Ohio Medicaid's managed care plans. Thus, prescription drug benefits for Medicare beneficiaries are affected by the same tools that private health insurance and Ohio Medicaid beneficiaries are. I now describe the tools that are commonly used by PBMs and the ODM and explain how they have been used with respect to the Teva and Actavis Generic Defendants' opioid products. I show that the Teva and Actavis Generic Defendants' generic opioid products have been covered generously by third party health plans throughout the period of the allegations, and that more significant restrictions on coverage could have been imposed to control usage of these drugs.

1. Overview of Health Insurance Formularies

79. A formulary "is a list of drugs favored by the PBM for their clinical effectiveness and cost savings."[157] Formularies range from open to closed, with open formularies amounting to a "list of recommended drugs," and closed formularies "limit[ing] reimbursement to those drugs listed on the formulary."[158] In practice, most formularies lie somewhere in between—incented

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[154] "How to Get Drug Coverage," *Medicare.gov*, available at https://www.medicare.gov/drug-coverage-part-d/how-to-get-drug-coverage, accessed February 15, 2019.
[155] "How to Get Drug Coverage," *Medicare.gov*, available at https://www.medicare.gov/drug-coverage-part-d/how-to-get-drug-coverage, accessed February 15, 2019; "How Do Medicare Advantage Plans Work?" *Medicare.gov*, available at https://www.medicare.gov/sign-up-change-plans/types-of-medicare-health-plans/medicare-advantage-plans/how-do-medicare-advantage-plans-work.
[156] John K. Gorman et al., "Chapter 24: Health Plans and Medicare" in *Essentials of Managed Health Care,* Sixth Edition, ed. Peter R. Kongstvedt (Burlington, MA: Jones & Bartlett Learning, 2013), pp. 501–506.
[157] Study of Pharmaceutical Benefit Management, p. 9.
[158] Study of Pharmaceutical Benefit Management, p. 18.

formularies, which "appl[y] differential co-pays or other financial incentives to influence patients to use, pharmacists to dispense, and physicians to write prescriptions for formulary products."[159]

80. "Many commercial and Medicare Part D formularies use a three-tier formulary for nonspecialty drugs" with "generic drugs on tier one, preferred brand name drugs on tier two, and nonpreferred drugs on tier three."[160] The tier two drugs may be preferred either because they are "clinically superior" or have a low net cost to the insurer, in turn because of a low list price or a high negotiated rebate.[161] Copayments (fixed fees per filled prescription) and coinsurance (the percentage of the prescription cost that is paid by the patient) vary across the tiers to encourage patients to use lower-tier drugs.[162] There are many exceptions to the three-tier structure, with some plans, for example, dividing the generic tier into preferred and non-preferred generics.[163]

81. Formularies are designed by P&T committees.[164] The most important concerns of the P&T committee have traditionally been "the documented safety and efficacy of new drug formulations," but cost has become an important consideration as well, as healthcare spending continues to rise.[165] In some cases, the clinical and cost components are considered by separate entities.[166]

82. Similar to private plans, the ODM maintains a preferred drug list ("PDL").[167] A PDL is a list of drugs that a health plan covers without the need for prior authorization.[168] The ODM's PDL is developed by its P&T committee, which maintains the PDL "through a review of current evidence-based medicine and based upon the[ir] professional judgment."[169]

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[159] Study of Pharmaceutical Benefit Management, p. 18.
[160] Prescription Drug Benefits in Managed Care, p. 268.
[161] Prescription Drug Benefits in Managed Care, p. 268.
[162] Prescription Drug Benefits in Managed Care, p. 268.
[163] Prescription Drug Benefits in Managed Care, p. 268.
[164] Zhixiao Wang et al., "Cost-Effectiveness Analysis and the Formulary Decision-Making Process," *Journal of Managed Care Pharmacy* 10, no. 1, 2004, pp 48–59 at p. 48.
[165] Zhixiao Wang et al., "Cost-Effectiveness Analysis and the Formulary Decision-Making Process," *Journal of Managed Care Pharmacy* 10, no. 1, 2004, pp 48–59 at p. 48.
[166] See, e.g., "Formulary Development and Management at CVS Caremark," *CVS Caremark*, 2018, pp. 2–3
[167] "Pharmacy & Therapeutics (P&T) Committee," *Ohio Department of Medicaid*, available at https://pharmacy.medicaid.ohio.gov/pharmacy-therapeutics-committee, accessed May 2, 2019.
[168] "States Reporting Managed Care Pharmacy Uniform Preferred Drug List (PDL) Requirements," *KFF*, available at https://www.kff.org/medicaid/state-indicator/states-reporting-managed-care-pharmacy-uniform-preferred-drug-list-pdl-requirements/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D, accessed on May 2, 2019.
[169] "Pharmacy & Therapeutics (P&T) Committee," *Ohio Department of Medicaid*, available at https://pharmacy.medicaid.ohio.gov/pharmacy-therapeutics-committee, accessed May 2, 2019.

83. Formularies and PDLs are often subject to a number of restrictions, whereby patients will only have access to the drugs on the formularies at the listed copayments if certain conditions are met. PBMs can use these conditions to limit access to drugs, often by ensuring that other drugs are prescribed first or that other conditions are met. These types of restrictions, discussed next, are ways in which PBMs influence the drugs that are prescribed by doctors and that are ultimately used by patients.

2. TPPs Could Have Used Prior Authorization Restrictions More Effectively to Discourage the Prescribing of the Teva and Actavis Generic Defendants' Opioid Products

84. One of the common tools used by PBMs to limit prescriptions is prior authorization ("PA") restrictions. Prescription drugs that are subject to prior authorization restrictions must be reviewed and approved by health insurance carriers before they are covered by prescription drug plans.[170] This often involves "ask[ing] the physician about diagnostic tests, symptoms, and other clinical measures [to] establish the appropriateness of" the prescription before authorizing its reimbursement.[171]

85. PA is commonly used, for example, to limit off-label uses of a drug when the insurer prefers to reimburse other therapies instead. The HCFA *Study of Pharmaceutical Benefit Management* lists "major off-label uses not approved by the Food and Drug Administration" as an important factor in requiring PA.[172] This is also discussed by the Academy of Managed Care Pharmacy:

> Health plans may limit coverage of drugs to FDA-approved uses, or for unapproved, or off-label, uses that are supported by adequate medical evidence.…Prior authorization can be used for drugs that have a high propensity to be prescribed for unapproved use. Requests for approval of an off-label use of a drug would normally require documentation of the use for which it is prescribed. If the indication for the drug were not FDA-approved, the plan would either require the prescriber to present evidence or would ask the pharmacist to conduct

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[170] "What is Prior Authorization and How Does the Process Work?" *Cigna*, July 2018, available at https://www.cigna.com/individuals-families/understanding-insurance/what-is-prior-authorization, accessed January 3, 2019.
[171] Study of Pharmaceutical Benefit Management, p. 82.
[172] Study of Pharmaceutical Benefit Management, p. 82.

> a medical literature review to find evidence for the unapproved use. In this situation, the pharmacist would need to evaluate the documentation to determine whether use of the prescribed drug for the indication provided is justifiable.[173]

86. Drugs that may be abused frequently require PA. In explaining to its members how PA policies are formulated, Cigna notes that some medications subject to PA "[a]re very addictive" or "are often misused or abused."[174] The Academy of Managed Care Pharmacy specifically discusses narcotic analgesics, noting that PA can be used in concert with quantity limits, discussed below, "to offer exceptions to maximum dosing limits for patients with certain chronic pain conditions such as those caused by terminal cancer."[175]

87. To analyze the prevalence of PA restrictions, I obtained data from Fingertip Formulary, a resource provided by Decision Resources Group. This database compiles information on the formulary design of over 7,000 health plans in the U.S., though many of these may represent substantially the same plan at different points in time, but with different identifiers. I obtained data from Fingertip Formulary from April 2009 through September 2015. I have information on the state in which a plan is active; the tier of the drug; and any restrictions on the drug for the Teva and Actavis Generic Defendants' opioid drugs at issue. I restrict analysis of Fingertip Formulary data in this report to plans that are operative in Ohio.

88. **Exhibit 4** shows the frequency of PA restrictions on the Teva and Actavis Generic Defendants' opioid drugs using the Fingertip Formulary database in both Medicare, Ohio Medicaid managed care and private health insurance plans. The Exhibit separately considers Actiq, Fentora, and generic opioids.[176] As can be seen, only 25 percent to 40 percent of health plans had PA restrictions on Actiq and Fentora between the second quarter of 2009 and the third quarter of 2015, while on average only 5 percent to 10 percent had PA restrictions on generic opioids. That is, the large majority of health plans did not have PA restrictions on Actiq,

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[173] "Prior Authorization and the Formulary Exception Process," *AMCP*, available at http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9795.
[174] "What is Prior Authorization and How Does the Process Work?" *Cigna*, July 2018, available at https://www.cigna.com/individuals-families/understanding-insurance/what-is-prior-authorization, accessed January 3, 2019.
[175] "Prior Authorization and the Formulary Exception Process," *AMCP*, available at http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9795.
[176] In all Fingertip Formulary analyses, I restrict attention to only those generic opioids for which the Teva or Actavis Generic Defendants make a version.

Fentora, and generic opioids during this period, thereby providing insurance coverage for even off-label use.

89. The ODM uses PA "to ensure the safety of [its] beneficiaries and to help control costs."[177] In general, the ODM requires PA for name-brand prescription drugs when generics are available.[178] As of October 1, 2017, the State of Ohio has required all Ohio Medicaid plans to require prior authorization for long-acting opioid pain medications.[179]

90. According to Fingertip Formulary data Ohio Medicaid fee-for-service had PA restrictions in place for Actiq and Fentora throughout the period considered in my analysis. However, for the majority of the period considered, more than half of generics manufactured by the Teva and Actavis Generic Defendants had no PA restrictions in place. In fact, in the first quarter of 2010 more than 80 percent of the Teva and Actavis Generic Defendants' generic opioids did not require prior authorization. Even through the third quarter of 2015, more than 40 percent of generic opioids were available without prior authorization. This limited use of PA by third party health plans shows that these parties could have taken but failed to take more aggressive measures to curb opioid prescriptions.

91. As explained earlier in this report, payors and PBMs had knowledge of the risks of opioid abuse during the period of the allegations; thus, lack of awareness could not have prevented these payors from taking more aggressive measures. Moreover, as I discuss later, academic research has found that tools used by managed care can have a significant impact on prescribing behavior.

3. TPPs Could Have Used Step Therapy Restrictions More Effectively to Reduce the Prescribing of the Teva and Actavis Generic Defendants' Opioid Products

92. The Academy of Managed Care Pharmacy describes step therapy as an "approach to care [that] requires the use of a recognized first-line drug before approval of a more complex second-

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[177] "Prior Authorization (PA) Information," *Ohio Department of Medicaid*, available at https://pharmacy.medicaid.ohio.gov/prior-authorization, accessed May 2, 2019.
[178] "Ohio Medicaid Covered Services," *Ohio Department of Medicaid*, available at https://medicaid.ohio.gov/FOR-OHIOANS/Covered-Services#1683595-prescriptions, accessed May 2, 2019.
[179] "Caresource Implements Quality Limits on Opioids for Ohio Medicaid," CareSource, 2018, available at https://www.caresource.com/documents/oh-p-1413_spring2018-providersource-insert-mcd-opiod-04042018/.

line drug is given."[180] This traditionally requires patients to try a generic before approval is granted to reimburse a more expensive branded drug in the same therapeutic class.[181] However, it could be used to require patients to attempt to control their pain with medications that carry a lower risk of abuse before being granted approval to use opioids. For example, patients could first be treated using nonsteroidal anti-inflammatory drugs ("NSAIDs"), a class of OTC pain relievers. Only after NSAIDs failed to be effective would patients be prescribed opioids as the next step of their pain management.[182]

93. **Exhibit 5** shows the percentage of private, Ohio Medicaid managed care, and Medicare health plans with step therapy requirements for the Teva and Actavis Generic Defendants' opioid products for the period between the second quarter of 2009 and the third quarter of 2015. As can be seen in the Exhibit, only a small share of health plans have such restrictions: Less than 2 percent of plans had step therapy on generic opioids, and between 3 percent and 6 percent of plans had step therapy on Actiq and Fentora. Similarly, fee-for-service Ohio Medicaid never imposed step therapy on Actiq or Fentora during the period I analyzed, and it did not begin imposing step therapy on generic opioids until 2013; by the end of the third quarter of 2015 more than two thirds of generics remained available without step therapy.

94. The limited use of this tool shows that TPPs could have taken, but failed to take, more effective measures to curb opioid prescriptions. This is also true with respect to quantity limits, as discussed next.

4. TPPs Could Have Used More Stringent Quantity Limits to Limit the Utilization of the Teva and Actavis Generic Defendants' Opioid Products

95. PBMs often impose limits on the quantities of certain drugs that will be reimbursed. Quantity limits are generally imposed on specific prescription drugs for safety or cost reasons,

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[180] "Prior Authorization and the Formulary Exception Process," *AMCP*, available at http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=9795.
[181] Brenda R. Motheral, "Pharmaceutical Step-Therapy Interventions: A Critical Review of the Literature," *Journal of Managed Care Pharmacy* 17, no. 2, 2011, pp. 143–155 at pp. 143–144.
[182] "Health Insurance Plans May Be Fueling Opioid Epidemic," *Johns Hopkins Bloomberg School of Public Health*, June 22, 2018, available at https://www.jhsph.edu/news/news-releases/2018/health-insurance-plans-may-be-fueling-opioid-epidemic.html, accessed January 8, 2019.

and can be used to reduce the risk of overuse.[183] As an example of such a policy, consider the one CVS Caremark introduced in 2018 for opioids.[184] It places limits on the duration of therapy for new, acute conditions, the total morphine milligram equivalent ("MME") dose that can be reimbursed without PA, and the (higher) total MME dose that can be reimbursed with PA. Such limits would have better equipped insurers to control and manage appropriate use of opioids. I note that "employers and insurers can opt out of the program."[185]

96. **Exhibit 6** shows data from Fingertip Formulary on the percentage of private, Ohio Medicaid managed care, and Medicare health plans that have quantity limits. The Exhibit shows that roughly between 15 percent and 45 percent of health plans imposed quantity limits on Actiq, Fentora, and generic opioids. Quantity limits gradually became more prevalent for generic opioids. Ohio Medicaid fee-for-service did not have quantity limits in place for Actiq and Fentora during the period I analyzed, but did generally increase the proportion of generic opioids with quantity limits over time. On October 1, 2017, the State of Ohio required all Ohio Medicaid plans to place quantity limits on short-acting opioid prescriptions as part of "continuing efforts to fight opioid abuse."[186]

97. As such, the majority of health plans did not have quantity limits between the second quarter of 2009 and the third quarter of 2015; thus, these plans forewent a tool that they could have used during the period to curb opioid abuse.

5. Plaintiffs Could Have Taken More Aggressive Measures to Reduce Opioid Abuse, But Chose Not to

98. Not only did private payors and other TPPs fail to take more aggressive measures to reduce opioid abuse—so did Plaintiffs. Cuyahoga County, for instance, did not make rigorous

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[183] "Quantity Limits," *Medicare.gov*, available at https://www.medicare.gov/node/39146; "Quantity Limits — Core and Select," *OptumRx*, January 1, 2019, available at http://doa.alaska.gov/drb/benefits/materials/AlaskaCarePharmacy_QuantityLimits.pdf.
[184] "CVS Caremark Opioid Quantity Limits Pharmacy Reference Guide," *CVS Caremark*, 2018, available at https://www.caremark.com/portal/asset/Opioid_Reference_Guide.pdf.
[185] Andrew Joseph, "CVS Tightens Restrictions on Opioid Prescriptions in Bid to Stanch Epidemic," *Statnews*, September 21, 2017, available at https://www.statnews.com/2017/09/21/cvs-opioid-prescription-limits/, accessed February 15, 2019.
[186] "CareSource Implements Quantity Limits on Opiods for Ohio Medicaid," *CareSource*, available at https://www.caresource.com/documents/oh-p-1413_spring2018-providersource-insert-mcd-opiod-04042018/.

use of formulary tools in order to curb opioid use. Holly Woods, the director of Human Resources for Cuyahoga County who was responsible for considering design changes to the medical health and prescription drug plans,[187] testified that she was "not aware" of whether the county had taken any measures to determine "if any[] of the opioid medications covered under its [employee healthcare] plans was not medically necessary."[188] Furthermore, she additionally testified that although the county has "the sole authority to make changes to the coverage" of the healthcare plans that it offers to employees,[189] she was "not aware" of the county asking to place limitations on the types of opioids covered by plan providers,[190] such as prior authorization.[191]

99. Likewise, June Carr, Summit County's Deputy Director of Employee Benefits, testified on behalf of Summit County that she is unaware that the County ever asked any PBM to implement prescription opioid utilization management tools, much less requested any changes concerning the County's the coverage of prescription opioids under its health plans.[192] As a result, the County continues to pay for opioid prescriptions for chronic pain to this day.[193]

C. The Tools Available to Third Party Payors Significantly Influence Prescription Drug Use. Thus, If Used More Often and Earlier, Plaintiffs and Third-Party Payors Could Have Limited Opioid Use in Ohio

100. In this section, I discuss evidence that greater restrictions by payors reduce the amount of that drug that is prescribed and consumed. If a negative causal link between payor restrictions and drug prescriptions can be established, one can conclude that, had payors been more restrictive as discussed above, they would have reduced the extent of the opioid prescribing and, therefore, any alleged damages.

101. Important evidence comes from academic studies, many of which find that prescription drug benefits affect physician prescribing behavior. Mager et al. examine the effect of plan design on the likelihood that patients fill prescriptions with generics, finding that "several plan

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[187] September 27, 2018 Deposition of Holly Woods, 28:8–29:8.
[188] September 27, 2018 Deposition of Holly Woods, 254:10–254:23.
[189] September 27, 2018 Deposition of Holly Woods, 275:22–277:2.
[190] September 27, 2018 Deposition of Holly Woods, 41:3–10, 42:8–10, 91:17–92:5, 94:10–22, 111:25–112:11.
[191] January 7, 2019 Deposition of Holly Woods, at 33:16–25.
[192] 12/21/2018 Depositionof June Carr, at 155:21–156:25.
[193] *Id.*

design factors significantly and positively influenced the probability of filling generic prescriptions. These included step therapy, prescription drug benefit type, and generic/preferred-brand copayment differential."[194] This suggests that more preferred and less restricted drugs are more likely to be consumed by patients.

102. Research has also found that out-of-pocket costs ("OOP") affect opioid consumption. For example, Soni uses the introduction of Medicare Part D to test whether a reduction in OOP costs leads to increased opioid usage.[195] She finds that if out-of-pocket costs fall by 10 percent, patients tend to increase their opioid consumption by 8.9 percent in terms of days' supply.[196] Once the strength of the opioid dispensed is considered, the increase in opioid consumption is 11.2 percent when out-of-pocket costs fall by 10 percent.[197] Non-opioid painkillers exhibited no statistically significant response to the reduction in out-of-pocket costs.[198]

103. Other works confirm these findings. For example, David Powell and coauthors perform a similar investigation and find that the introduction of Medicare Part D reduced eligible patients' OOP costs for opioids by 47.6 percent while increasing their opioid prescriptions by 28 percent.[199] This highlights an important way in which drugs became cheaper over the period of allegations, even if formulary tiers are not considered: Medicare Part D was introduced, which led to reduced OOP costs for those over 65. My research with Kosali Simon also found that increases in OOP costs lead to a decrease in prescriptions.[200] Soni's paper mentioned above lists many other research articles estimating a negative relationship between OOP and prescriptions. In sum, there is ample evidence that increasing OOP costs of prescription drugs, including of

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[194] Douglas E. Mager and Emily R. Cox, "Relationship Between Generic and Preferred-Brand Prescription Copayment Differentials and Generic Fill Rate," *The American Journal of Managed Care*, 13, no. 6, 2007, pp. 347–352.

[195] Aparna Soni, "Health Insurance, Price Changes, and the Demand for Pain Relief Drugs: Evidence from Medicare Part D," working paper, September 25, 2018.

[196] Aparna Soni, "Health Insurance, Price Changes, and the Demand for Pain Relief Drugs: Evidence from Medicare Part D," working paper, September 25, 2018, pp. 17, 42.

[197] Aparna Soni, "Health Insurance, Price Changes, and the Demand for Pain Relief Drugs: Evidence from Medicare Part D," working paper, September 25, 2018, p. 42.

[198] Aparna Soni, "Health Insurance, Price Changes, and the Demand for Pain Relief Drugs: Evidence from Medicare Part D," working paper, September 25, 2018, p. 42.

[199] David Powell et al., "How Increasing Medical Access to Opioids Contributes to the Opioid Epidemic: Evidence from Medicare Part D," working paper, April 2017, p. 15.

[200] Jonathan D. Ketcham and Kosali I. Simon, "Medicare Part D's Effects on Elderly Patients' Drug Costs and Utilization," *American Journal of Managed Care* 14, no. 11, 2008, pp. SP14–SP22 at p. SP14.

opioids, leads to a decrease in prescriptions and usage. This means that third party payors could have placed opioids on higher tiers (with higher OOP costs), in order to decrease opioid prescriptions.

104. PA requirements also have been found to affect prescriptions. Marcus Dillender finds that introducing PA for some drugs for workers' compensation beneficiaries reduces the likelihood of those beneficiaries receiving a prescription for a non-preferred drug by almost 50 percent.[201] Furthermore, he finds that "physicians appear to substitute to preferred drugs" rather than reduce prescribing in the aggregate.[202] This indicates that the PA requirement is a useful tool for influencing prescriber behavior. He also found that PA requirements reduced the likelihood of receiving benzodiazepines in conjunction with opioids, a dangerous combination.[203] Such formulary restrictions could be written with the intent of discouraging or preventing the dangerous use of drugs, such as patterns of opioid prescribing that lead to abuse.

105. Additionally, as Margolis et al. conclude, PA requirements influence and control access to a specific drug and direct patients to alternative therapies.[204] In the present context, this means that placing PA requirements on opioids, but leaving other pain therapies without a PA requirement, could lead to reduced usage of opioids.

106. Other research identifies additional factors that amplify the effect of formulary policies. The first is spillover effects. Physicians who treat many patients for whom a drug is not preferred prescribe less of that drug—even to their patients for whom it *is* preferred.[205] This suggests formulary policies alter physicians' prescribing behaviors. In my own research, I have found that Medicaid preferred drug lists affect drug choice for both Medicaid and non-Medicaid

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[201] Marcus Dillender, "What Happens When the Insurer Can Say No? Assessing Prior Authorization as a Tool to Prevent High-Risk Prescriptions and to Lower Costs," *Journal of Public Economics*, 165, 2018, pp. 170–200 at p. 171.

[202] Marcus Dillender, "What Happens When the Insurer Can Say No? Assessing Prior Authorization as a Tool to Prevent High-Risk Prescriptions and to Lower Costs," *Journal of Public Economics*, 165, 2018, pp. 170–200 at p. 171.

[203] Marcus Dillender, "What Happens When the Insurer Can Say No? Assessing Prior Authorization as a Tool to Prevent High-Risk Prescriptions and to Lower Costs," *Journal of Public Economics*, 165, 2018, pp. 170–200 at p. 187.

[204] Jay M. Margolis et al., "Effects of a Medicaid Prior Authorization Policy for Pregabalin," *The American Journal of Managed Care* 15, no. 10, 2009, pp. e95–e102 at p. e101.

[205] Y. Richard Wang and Mark V. Pauly, "Spillover Effects of Restrictive Drug Formularies on Physician Prescribing Behavior: Evidence from Medicaid," *Journal of Economics & Management Strategy* 14, no. 3, 2005, pp. 755–773 at p. 755.

patients. Specifically, my research showed that in an anonymous survey of primary care physicians and cardiologists in nine states with preferred drug lists, 30 percent of physicians indicated that Medicaid preferred drug lists decreased the probability that they would prescribe drugs that were not covered by the preferred drug lists to non-Medicaid patients.[206] This means that formulary policies influence prescribing behavior for patients not directly covered by that specific policy. Therefore, changes in Medicaid policy affect physicians' behavior towards their other patients not enrolled in Medicaid.

107. A second, and similar, amplifying factor is diversion of drugs "from their lawful purpose into illicit drug traffic."[207] Powell et al. found a link between the insurance coverage of opioids for some patients, and the symptoms of opioid abuse *outside* those patients. In particular, they show that the increased prescription drug coverage obtained by seniors when Medicare Part D was launched led to increases in the opioid supply in states with large elderly populations, which in turn resulted in an "increase in opioid-related deaths among the Medicare-ineligible population, suggesting substantial diversion from medical markets."[208] This indicates that formulary design plays a broad role in determining opioid consumption and subsequent alleged damages, even among the population not covered by the formulary itself.

108. A third factor amplifying the effect of formulary policies is information technology, which affects the ease with which a physician can look up relevant information regarding formulary policy. In particular, I have found in my own research that "when physicians are provided with formulary information, PA requirements imposed by PBMs influence their prescribing decisions more than pharmaceutical firms' promotional efforts."[209] In essence, when physicians are made more aware of formulary restrictions, the effect on prescribing behavior is more impactful. Ultimately my research indicated "that greater efforts to provide patient-

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[206] Jonathan D. Ketcham and Andrew J. Epstein, "Which Physicians are Affected Most by Medicaid Preferred Drug Lists for Statins and Antihypertensives?" *PharmacoEconomics* 24, no. 3, 2006, pp. 27–40 at p. 33.
[207] "Diversion Control Division," *DEA*, available at https://www.dea.gov/diversion-control-division, accessed January 18, 2019.
[208] David Powell et al., "How Increasing Medical Access to Opioids Contributes to the Opioid Epidemic: Evidence from Medicare Part D," working paper, April 2017, p. 1.
[209] Andrew J. Epstein and Jonathan D. Ketcham, "Information Technology and Agency in Physicians' Prescribing Decisions," *The RAND Journal of Economics* 45, no. 2, 2014, pp. 422–448 at p. 438.

specific formulary information to physicians at the point of care would alter physicians' prescribing decisions, and in particular would enhance the influence of existing formularies."[210]

109. In sum, academic research shows that the tools available to third party payors can have a significant effect on prescription drug use. These tools could have been used more effectively to prevent or limit opioid use in Ohio.

D. TPPs Had a Financial Incentive to Cover Opioids over Other Methods of Treating Pain

110. Despite P&T committees' responsibilities to ensure that formularies promote patient well-being, as well as the fact that they are informed, TPPs and PBMs have a financial incentive to cover opioids generously relative to other methods of treating pain. This could explain the limited and delayed response to issues relating to opioid abuse. The overall business model of PBMs, academic literature, and anecdotal evidence from news articles all suggest that PBMs' and TPPs' financial incentives have made them less likely to mitigate inappropriate opioid usage.

111. PBMs have a financial incentive to maximize the number of prescriptions covered because their business is heavily volume driven in multiple ways. First, PBMs make money on the difference between the price they charge plan sponsors for drugs and the price they pay for drugs.[211] The more filled prescriptions a PBM administers, the higher profit they earn. The money made from this spread, particularly on generic drugs, represents a large portion of PBM profits.[212] For example, a 2018 audit of Ohio PBMs found that Medicaid PBMs in Ohio charged a 31% spread for generic drug prescriptions over the period April 1, 2017 to March 31, 2018 (and a 9% spread across all drugs).[213] In response to these findings, Ohio required its Medicaid

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[210] Andrew J. Epstein and Jonathan D. Ketcham, "Information Technology and Agency in Physicians' Prescribing Decisions," *The RAND Journal of Economics* 45, no. 2, 2014, pp. 422–448 at p. 439.
[211] Patricia M. Danzon, "Pharmacy Benefit Management: Are Reporting Requirements Pro- or Anticompetitive?," *International Journal of the Economics of Business* 22, no. 2, 2015, pp. 245–261 at p. 248.
[212] Martha M. Rumore and F. Randy Vogenberg, "PBM P&T Practices: The HEAT Initiative is Gaining Momentum," *Health Care & Law* 42, no. 5, 2017, pp. 330–335 at p. 332.
[213] Ohio Auditor of State Press Release, "Auditor's Report: Pharmacy Benefit Managers Take Fees of 31% on Generic Drugs Worth $280M in One-Year Period," August 16, 2018, available at https://ohioauditor.gov/news/pressreleases/Details/5042, accessed May 2, 2019.

managed care plans to terminate their spread-based PBM contracts in January 2019, and to switch from spread-based pricing models to pass-through models.[214]

112. Second, a PBM's negotiation position is strengthened by any increase in market share; if it can generate higher volume for drug manufacturers, it can negotiate discounts on drug prices from those manufacturers.[215] PBMs' market shares can be enhanced by two factors, both of which result from more generous coverage. First, more generous coverage leads to a higher volume of prescriptions per covered life.[216] This occurs because patients' out-of-pocket costs are important determinants of prescription drug use. Second, more generous coverage, conditional on premiums, increases the number of covered lives as the plan design becomes more attractive to consumers and their agents (such as employers' human resource departments). In turn, PBMs can turn these discounts into higher profits either directly, or by passing the discounts onto plan sponsors, thereby increasing the appeal of their offering to those sponsors. Thus, PBMs have significant incentives to err on the side of more liberal opioid coverage.

113. As a concrete example of how this phenomenon might affect opioid usage, Baker and coauthors showed that Medicare Advantage plans reduce the likelihood of filling an opioid prescription, relative to stand-alone prescription drug plans.[217] This may be a result of properly aligned incentives; Medicare Advantage plans are responsible for non-pharmaceutical medical benefits, but stand-alone prescription drug plans are not. Thus, Medicare Advantage plans had more incentive to consider holistic health outcomes when developing formularies.

114. Evidence that these financial incentives may be leading TPPs and PBMs to avoid taking the steps discussed above to mitigate opioid use is not limited to academia; anecdotal evidence from news articles and policy experts also shows this. For example, one patient used Butrans to control abdominal pain before UnitedHealthcare stopped covering the drug. At that point, she felt compelled to switch to morphine, a drug that the DEA says carries a much higher risk of

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[214] "Ohio Medicaid Announces Plans for Significant Reforms to Pharmacy Program," *Ohio Pharmacists*, available at https://www.ohiopharmacists.org/aws/OPA/pt/sd/news_article/183671/_PARENT/layout_interior_details/false, accessed on May 2, 2019.

[215] "Health Policy Brief: Pharmacy Benefit Managers," *Health Affairs*, September 14, 2017, available at available at https://www.healthaffairs.org/do/10.1377/hpb20171409.000178/full/.

[216] "Health Policy Brief: Pharmacy Benefit Managers," *Health Affairs*, September 14, 2017, available at https://www.healthaffairs.org/do/10.1377/hpb20171409.000178/full/.

[217] Baker et al., "The Effects of Medicare Advantage on Opioid Use," *NBER Working Paper Series*, December 2018.

abuse, addiction, and overdose.[218] The same article quotes Dr. Thomas R. Frieden, former Director of the CDC, as saying that "insurance companies, with few exceptions, had 'not done what they need to do to address' the opioid epidemic," while "Leo Beletsky, an associate professor of law and health sciences at Northeastern University, went further, calling the insurance system 'one of the major causes of the crisis' because doctors are given incentives to use less expensive treatments that provide fast relief."

115. Another article also concludes that while a combination of education and proper exercise may be the best solution to back pain, health plans pay for "non-evidence-based interventions like opioids and make it difficult and expensive for patients to access evidence-based interventions such as physical therapy" because there is "far more profit in pills than physical therapy."[219]

VI. Plaintiffs and Plaintiffs' Experts Incorrectly Consider the Role that the State of Ohio Has in Preventing Opioid Abuse

116. Plaintiffs and Plaintiffs' experts do not appropriately consider the role that the State of Ohio has in preventing opioid abuse. For example, Professor Gruber states that prescription drug monitoring programs ("PDMPs") worsened the opioid epidemic by causing individuals addicted to prescription opioids to switch to illicit substances such as fentanyl and heroin starting around 2010.[220] Additionally, Plaintiffs and Plaintiffs' experts do not recognize the ability that states have, including the State of Ohio, to reduce problems with opioid abuse by facilitating access to treatment for opioid dependence and overdose. This is discussed next.

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[218] Katie Thomas and Charles Ornstein, "Amid Opioid Crisis, Insurers Restrict Pricey, Less Addictive Painkillers," *The New York Times*, available at https://www.nytimes.com/2017/09/17/health/opioid-painkillers-insurance-companies.html.
[219] Dave Chase, "The Opioid Crisis is Partly Fueled by Insurers' and Employers' Approach to Back Pain," *STAT*, March 27, 2019.
[220] Gruber Report, ¶¶ 42, 46–52, 55.

A. The State of Ohio Could Have Implemented a Prescription Drug Monitoring Program Sooner than It Did, and It Could Have Had More Stringent Requirements

1. Overview of Prescription Drug Monitoring Programs and Implementation in Ohio

117. State governments can use PDMPs to manage prescriptions for controlled substances. According to the CDC, a PDMP "is an electronic database that tracks controlled substance prescriptions in a state. PDMPs can provide health authorities timely information about prescribing and patient behaviors…and facilitate a nimble and targeted response."[221] More specifically, pharmacists enter dispensing data into the database, and prescribers can—or, in some cases, must—query that database before writing a prescription for a controlled substance. While PDMPs have existed since the 1930s, there has been a resurgence of them since the early 2000s as states have attempted to limit opioid usage.[222]

118. PDMPs are differentiated by the mandates on reporting and querying that state legislatures associate with them. PDMPs were originally devised to assist law enforcement and tracked Schedule II substances.[223] Therefore, their early construction was focused on *reporting* the dispensing of these substances, rather than querying of the database by prescribers or dispensers. In fact, according to a review of PDMP policies, in 1998, less than one third of states with PDMPs even *allowed* "physicians or pharmacists to access patient-identifiable data,"[224] and mandates centered on the frequency with which dispensing data be submitted. By 2011, when that review closed, almost all states had "extended access to physicians and…pharmacists," and

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[221] "What States Need to Know about PDMPs," *CDC*, October 3, 2017, available at https://www.cdc.gov/drugoverdose/pdmp/states.html.
[222] Yuhua Bao et al., "Prescription Drug Monitoring Programs Are Associated with Sustained Reductions in Opioid Prescribing by Physicians," *Health Affairs* 35, no. 6, 2016, pp. 1045–1051 at p. 1045.
[223] "History of Prescription Drug Monitoring Programs," Prescription Drug Monitoring Program and Training and Technical Assistance Center Technical Assistance Guide, March 2018, p. 4; Corey S. Davis et al., "Evolution and Convergence of State Laws Governing Controlled Substance Prescription Monitoring Programs, 1998-2011," *American Journal of Public Health* 104, no. 8, 2014, pp. 1389–1395 at pp. 1390–1391. Later, states began to track the distribution of other schedules, but all drugs relevant to this litigation are Schedule II.
[224] Corey S. Davis et al., "Evolution and Convergence of State Laws Governing Controlled Substance Prescription Monitoring Programs, 1998-2011," *American Journal of Public Health* 104, no. 8, 2014, pp. 1389–1395 at p. 1392.

focus turned to whether those professions were *required* to access the database prior to prescribing or dispensing.[225]

119. Broadly, these querying mandates fall into two categories: registration mandates and use mandates.[226] Registration mandates require prescribers to register to use the program, while use mandates require prescribers to query the program before writing certain prescriptions.[227] States with use mandates have widely varying conditions: Some states require queries before every initial opioid prescription and with a recurring frequency, while others require it only if the physician subjectively suspects that the patient might be seeking opioids for nonmedical use.[228] The CDC suggests that PDMPs are most effective when physicians are required to check a patient's history; when pharmacists are required to enter information in real time; when health authorities actively review the data; and when they are prescriber friendly.[229]

120. In 2006, Ohio implemented a PDMP "collect[ing] information on all outpatient prescriptions for controlled substances… dispensed by Ohio-licensed pharmacies and personally furnished by Ohio prescribers."[230] The database is required to be updated every 24 hours; additionally drug wholesalers must report monthly data on all controlled substances sold to pharmacies and prescribers.[231] Ohio enacted a comprehensive use mandate effective in 2015.[232] Prior to that, regulations passed in 2011 only "required prescribers to review PDMP reports at the beginning of therapy and annually after that if they had reason to believe that treatment with controlled substances in Schedules II–V would extend beyond 12 weeks."[233] In 2014 a new law

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[225] Corey S. Davis et al., "Evolution and Convergence of State Laws Governing Controlled Substance Prescription Monitoring Programs, 1998-2011," *American Journal of Public Health* 104, no. 8, 2014, pp. 1389–1395 at p. 1392.
[226] Hefei Wen et al., "States with Prescription Drug Monitoring Mandates Saw Reduction in Opioids Prescribed to Medicaid Enrollees," *Health Affairs* 36, no. 4, 2017, pp. 733–741 at p. 734.
[227] Hefei Wen et al., "States with Prescription Drug Monitoring Mandates Saw Reduction in Opioids Prescribed to Medicaid Enrollees," *Health Affairs* 36, no. 4, 2017, pp. 733–741 at p. 734.
[228] Hefei Wen et al., "States with Prescription Drug Monitoring Mandates Saw Reduction in Opioids Prescribed to Medicaid Enrollees," *Health Affairs* 36, no. 4, 2017, pp. 733–741 at p. 735.
[229] "What States Need to Know about PDMPs," *CDC*, October 3, 2017, available at https://www.cdc.gov/drugoverdose/pdmp/states.html.
[230] "What is OARRS?" *The State of Ohio Board of Pharmacy*, available at https://www.ohiopmp.gov/About.aspx, accessed May 2, 2019.
[231] "What is OARRS?" *The State of Ohio Board of Pharmacy*, available at https://www.ohiopmp.gov/About.aspx, accessed May 2, 2019.
[232] "Prescription Drug Monitoring Programs: Evidence-Based Practices to Optimize Prescriber Use," The Pew Charitable Trusts Report, December 2016 ("Pew Report"), p. 17.
[233] Pew Report, p. 17.

required that "prescribers must request a PDMP report prior to the first opioid or benzodiazepine prescription and every 90 days after that" with certain exceptions.[234]

2. Prescription Drug Monitoring Programs With Certain Attributes Have Been Found Effective In Reducing Opioid Prescriptions And Abuse. These Attributes Could Have Been Implemented Earlier In Ohio

121. Professor Gruber claims that the introduction of PDMPs worsened the opioid epidemic by causing individuals addicted to prescription opioids to switch to illicit substances such as fentanyl and heroin starting around 2010.[235] First, as Schuchat et al. (2017) note, "[t]here is no evidence that state policies designed to reduce inappropriate opioid prescribing are leading to increases in heroin use and deaths from illicit opioid use."[236] Citing Dowell et al. (2016),[237] they go on to state that, "[i]n fact, such policies have been shown to reduce the amount of opioids prescribed, prescription opioid–involved overdose deaths, and all opioid-involved deaths. Some evidence also suggests that these opioid prescribing policies may reduce heroin overdose deaths."[238] Second, as I will discuss later in this report, this appears to assume that Marketing Defendants are the sole cause of addiction to prescription opioids, and ignores other factors that have been shown to impact opioid use. Third, Professor Gruber's conclusion implies that Ohio would have been better off without a PDMP at all. However, as discussed below, PDMPs with certain features have been found to be effective at reducing opioid use. Professor Gruber does not consider the possibility that opioid use in Ohio would have been substantially reduced had PDMPs with certain attributes been implemented earlier than they were. This is discussed next.

122. Studies have found that PDMPs can be effective at reducing opioid prescriptions, but only if they are constructed with the correct mandates. In a literature review, Volkow and McLellan concluded, "[r]isks of diversion through doctor shopping are best mitigated by the full

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[234] Pew Report, p. 17.
[235] Gruber Report, ¶¶ 42, 46–52, 55.
[236] Anne Schuchat et al., "New Data on Opioid Use and Prescribing in the United States," *JAMA* 318, no. 5, 2018, pp. 425–426.
[237] D. Dowell et al., "Mandatory Provider Review and Pain Clinic Laws Reduce the Amounts of Opioids Prescribed and Overdoes Death Rates," *Health Affairs* 35, no. 10, pp. 1876–1883.
[238] Anne Schuchat et al., "New Data on Opioid Use and Prescribing in the United States," *JAMA* 318, no. 5, 2018 pp. 425–426.

participation of all prescribers in Prescription Drug Monitoring Programs."[239] Studies that look specifically at stronger PDMPs find significant effects. For example, Buchmueller and Carey found that "must access" PDMPs—PDMPs where state law "requir[es] providers to access the PDMP under certain circumstances prior to prescribing"—curtailed the misuse of opioids in Medicare Part D, where misuse is defined in several different ways: percentage of enrollees obtaining prescriptions from five or more prescribers; percentage of enrollees obtaining prescriptions from five or more pharmacies; or percentage of enrollees "obtaining more than seven months [sic] supply in each half-year" or "fill[ing] claims before the previous claim's days [sic] supply has been used."[240] Wen and coauthors investigated both registration and use mandates, and found that registration mandates were particularly effective in reducing Schedule II opioid use by Medicaid enrollees, measured as number of prescriptions per enrollee or amount of spending per enrollee.[241] The authors suggest this may be because registration mandates "typically apply to all licensed prescribers in a state," but use mandates "differ in terms of types of drugs and types of prescribers to which the mandate applies, the circumstances under which prescribers are mandated to use the system, and whether prescribers are to exercise their subjective judgment as to what constitutes inappropriate use in deciding whether to use the system," though they note that "[i]n recent years, use mandates have imposed increasingly broad and obligatory criteria."[242]

123. A study by Grecu and co-authors showed that PDMPs that require querying prior to prescribing significantly reduce opioid abuse, "as measured by substance abuse treatment admissions and mortality related to Rx drugs," especially among young adults, and may reduce abuse of other drugs as well.[243] On the other hand, studies that do not control for the specific

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[239] Nora D. Volkow and Thomas McLellan, "Opioid Abuse in Chronic Pain – Misconceptions and Mitigation Strategies," *The New England Journal of Medicine* 374, no. 13, 2016, pp. 1253–1263, at p. 1258.
[240] Thomas C. Buchmueller and Colleen Carey, "The Effect of Prescription Drug Monitoring Programs on Opioid Utilization in Medicare," NBER Working Paper No. 23148, 2017, at pp. 2–4, 10.
[241] Hefei Wen et al., "States with Prescription Drug Monitoring Mandates Saw Reduction in Opioids Prescribed to Medicaid Enrollees," *Health Affairs* 36, no. 4, 2017, pp. 733–741.
[242] Hefei Wen et al., "States with Prescription Drug Monitoring Mandates Saw Reduction in Opioids Prescribed to Medicaid Enrollees," *Health Affairs* 36, no. 4, 2017, pp. 733–741.
[243] Anca M. Grecu et al., "Mandatory Access Prescription Drug Monitoring Programs and Prescription Drug Abuse," *Journal of Policy Analysis and Management* 38, no. 1, 2019, pp. 181–209 at p. 181.

mandates associated with a PDMP, but instead lump all of them together, find mixed effects.[244] In sum, PDMPs have been found to be effective at limiting the utilization of prescription opioids, but only if they are constructed with sufficiently strong provisions.

124. The PDMP that was implemented in Ohio had certain desirable elements, but could have adopted earlier the provisions that have been found to be useful in limiting opioid prescriptions. Specifically, as explained above, PDMPs where prescribers and dispensers are required to query the database before prescribing or dispensing are most effective at reducing opioid use and abuse. Starting in 2009 with Nevada, several states began to impose mandates that prescribers check the PDMP, but only if they had doubts about a patient's motives in seeking medication.[245] Mandates began to have fewer exceptions starting in the early 2010s. Kentucky passed a bill in 2012 that required prescribers, with a few exceptions, to check the PDMP before giving patients their first prescription for a Schedule II, III, or IV substance and every three months thereafter.[246] New York and Tennessee followed with similar regulations that took effect in 2013.[247] In all of these cases, opioid use fell rapidly in the respective states.[248] However, as discussed above, Ohio did not fully implement similar regulations until 2015.[249]

125. In sum, the State of Ohio could have implemented a stronger PDMP, and it could have done so earlier. Given the academic literature described above regarding early adopters of rigorous PDMP policies, evidence suggests that opioid abuse in Ohio would have been

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[244] Patrick and coauthors showed that the existence of any PDMP reduces opioid-related overdose deaths. See Stephen W. Patrick et al., "Implementation of Prescription Drug Monitoring Programs Associated with Reductions in Opioid-Related Death Rates," *Health Affairs* 35, no. 7, 2016, pp. 1324–1332 at p. 1324. Radakrishnan finds that the presence of a PDMP reduces "opioid abuse treatment admissions" and "suggestive evidence that PDMP's reduced non-medical use of prescription pain relievers…at the intensive margin." See Sharmini Radakrishnan, "The Impact of Information in Health Care Markets: Prescription Drug Monitoring Programs and Abuse of Opioid Pain Relievers," Working Paper, March 2014. Li and coauthors find that PDMPs are associated with *higher* opioid death rates, though there is no causal element to their analysis. See Guohua Li et al., "Prescription Drug Monitoring and Drug Overdose Mortality," *Injury Epidemiology* 1, no. 9, 2014, pp. 1–8. Meara and coauthors find no significant relationship between the presence of a PDMP and receipt or various measures of misuse of opioids. See Ellen Meara et al., "State Legal Restrictions and Prescription-Opioid Use among Disabled Adults," *The New England Journal of Medicine* 375, no. 1, 2016, pp. 44–53. And Brady and coauthors had mixed findings on the effect of PDMPs on dispensed morphine milligram equivalents (a measure of opioid strength) per capita. See Joanne E. Brady et al., "Prescription Drug Monitoring and Dispensing of Prescription Opioids," *Public Health Reports* 129, 2014, pp. 139–147.

[245] Pew Report, p. 8.

[246] Pew Report, p. 12.

[247] Pew Report, pp. 9, 15, 37.

[248] Pew Report, p. 9, 13, 17.

[249] Pew Report, p. 17.

substantially mitigated had the State employed a similarly rigorous program earlier. In Section IV above I discussed evidence that the State of Ohio was sufficiently informed regarding the risks associated with the Teva and Actavis Generic Defendants' opioid products to implement such regulation.

B. The State of Ohio Contributed to Problems with Opioid Abuse by Making it Difficult to Obtain Treatment for Opioid Dependence and Overdose

126. In addition to missing opportunities to curtail opioid prescriptions as described above, the State of Ohio enacted policies that made it difficult for people to receive treatment for opioid use disorder ("OUD") and opioid overdoses, exacerbating the impact of any excessive use in the State.

127. First, the State of Ohio failed to take steps that could have reduced the number of overdose deaths. These steps center on Ohio's policy toward naloxone, "a medication designed to rapidly reverse opioid overdose."[250] Naloxone "access laws" are valuable tools in preventing overdose deaths. Without such laws, naloxone is treated like any other prescription drug, requiring a prescription from a physician for the drug to be dispensed by a pharmacist to the patient in question.[251] However, access laws allow pharmacists to dispense naloxone outside these circumstances—to a third party like a friend or family member, or to the patient but without a prescription—getting the antidote into the hands of those most likely to be present when an overdose occurs.[252] New Mexico passed an access law in 2001, and Connecticut followed in 2003.[253] On the other hand, the State of Ohio did not pass an access law until 2014,[254] by which time 17 other states, including neighboring Kentucky, as well as many of the

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[250] "Opioid Overdose Reversal with Naloxone (Narcan, Evzio)," *National Institute on Drug Abuse*, April 2018, available at https://www.drugabuse.gov/related-topics/opioid-overdose-reversal-naloxone-narcan-evzio, accessed February 15, 2019.

[251] "Preventing the Consequences of Opioid Overdose: Understanding Naloxone Access Laws," Substance Abuse and Mental Health Services Administration, January 20, 2018, available at https://www.samhsa.gov/capt/sites/default/files/resources/naloxone-access-laws-tool.pdf

[252] "Preventing the Consequences of Opioid Overdose: Understanding Naloxone Access Laws," Substance Abuse and Mental Health Services Administration, January 20, 2018, available at https://www.samhsa.gov/capt/sites/default/files/resources/naloxone-access-laws-tool.pdf.

[253] "Naloxone Overdose Prevention Laws," *PDAPS*, July 1, 2017, available at http://pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139, accessed February 15, 2019.

[254] "Naloxone Overdose Prevention Laws," *PDAPS*, July 1, 2017, available at http://pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139, accessed February 15, 2019. I note that this law was

most populous states like California, New York, and Illinois, had passed access laws.[255] Additionally, through June 2017 Ohio continued to lack a law granting immunity from civil liability when administering naloxone.[256] This means that people experiencing overdoses, or those with them, may have been dissuaded from seeking or providing help in the event of an overdose for fear of being sued due to their actions, increasing the likelihood of an adverse outcome.

128. Additionally, federal policies meant it was much more difficult for persons with OUD to seek medically assisted treatment ("MAT"), defined by the Substance Abuse and Mental Health Services Administration. The federal requirements for coverage of buprenorphine, a chemical used to treat dependence,[257] are much stricter than those for many opioids. Specifically, "[i]n order to prescribe or dispense buprenorphine, physicians must qualify for a physician waiver, which includes completing eight hours of required training, and applying for a physician waiver."[258] Due to these restrictive regulations, there are a limited number of physicians eligible to write such prescriptions; in 2002 only 39 physicians in the State of Ohio were newly qualified to write such prescriptions, none of whom was certified to treat more than 100 patients.[259] In 2010, only 63 new physicians were certified.[260] By 2015, the number had risen to 157, of whom 109 could treat more than 100 patients.[261] Eventually, by 2018, that number had increased to 952

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implemented four years after the final report of the Ohio Prescription Drug Abuse Task Force. See "Ohio Prescription Drug Abuse Task Force: Final Report Task Force Recommendations," Wright State University CORE Scholar, https://corescholar.libraries.wright.edu/cgi/viewcontent.cgi?article=1007&context=prescription_drugs. At the time of the report, 6 states, including California, New York, and Illinois had passed naloxone access laws.

[255] "Naloxone Overdose Prevention Laws," *PDAPS*, July 1, 2017, available at http://pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139, accessed February 15, 2019.

[256] "Naloxone Overdose Prevention Laws," *PDAPS*, July 1, 2017, available at http://pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139, accessed February 15, 2019.

[257] "Buprenorphine," *Substance Abuse and Mental Health Services Administration*, May 31, 2016, available at https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine, accessed February 15, 2019

[258] "Buprenorphine Waiver Management," *Substance Abuse and Mental Health Services Administration*, available at https://www.samhsa.gov/medication-assisted-treatment/training-materials-resources/buprenorphine-waiver, accessed May 4, 2019.

[259] "Number of DATA-Waived Practitioners Newly Certified per Year," Substance Abuse and Mental Health Services Administration, available at https://www.samhsa.gov/medication-assisted-treatment/physician-program-data/certified-physicians?field_bup_us_state_code_value=OH, accessed May 2, 2019 ("Ohio DATA-Waived Practitioners").

[260] Ohio DATA-Waived Practitioners.

[261] Ohio DATA-Waived Practitioners.

physicians.[262] These restrictions meant that it was often more difficult for Ohioans to access MAT than additional opioids.

VII. Professor Rosenthal Ignores Several Factors that Influence Physician Prescribing Decisions

129. Plaintiff alleges "Defendants' conduct in promoting opioid use has had severe and far-reaching public health, social services, and criminal justice consequences" and that there are "extraordinary costs and losses that are directly related to Defendants' illegal actions."[263]

130. In an attempt to show causation and damages, Plaintiffs' experts take the following sequential steps:

- First Step: Plaintiff's expert, Professor Rosenthal, purports to "identify the extent to which the sale of prescription opioids…was caused by any quantum of the Defendants' promotional efforts that counsel can prove was unlawful."[264] In particular, she assumes that all promotion between 1995 and 2018 was unlawful and proposes two alternative estimates of the share of prescription opioid shipments that is attributable to misleading marketing.
- Second Step: Plaintiff's expert, Professor Cutler, then purports to use these alternative estimates by Professor Rosenthal to evaluate "the impact of prescription opioid shipments on harms that impose costs on Bellwether jurisdictions."[265]
- Third Step: The estimates from Professor Cutler's report are then used by Plaintiff's expert Professor McGuire to calculate the harms suffered by the Bellwether Counties from 2006–2016. In particular, Professor McGuire seeks to estimate past damages pertaining to the following five categories: mortality, morbidity, neonatal abstinence syndrome ("NAS"), crime, and child maltreatment.[266]

131. Professor Rosenthal purports to conduct a causation analysis between Marketing Defendants' alleged unlawful marketing and opioid shipments, and as explained above, her

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[262] Ohio DATA-Waived Practitioners.
[263] Complaint, ¶¶ 20–21.
[264] Expert Report of Meredith Rosenthal, March 25, 2019 ("Rosenthal Report"), ¶ 11.
[265] Expert Report of David Cutler, March 25, 2019 ("Cutler Report"), ¶¶ 8–9.
[266] Expert Report of Thomas McGuire (Damages to Bellwethers), March 25, 2019 ("McGuire Report"), ¶ 11.

analysis is used by other Plaintiffs' experts. Both her direct and indirect models, however, are not only flawed for the reasons discussed in Section XI and XII. They also ignore basic principles of prescribing behavior.

132. Her direct approach, discussed in more detail below, attempts to explain aggregate opioid shipments through a regression model where the independent variables are a measure of opioid prices and the aggregate stock of detailing.[267] This model is overly simplistic in that it ignores that physician prescribing decisions are influenced by many factors aside from prices and marketing—i.e., factors completely independent of the Teva and Actavis Generic Defendants' alleged conduct. In particular, physician prescribing decisions and, in turn, opioid shipments—the variable Professor Rosenthal analyzes—are influenced, among other factors, by scientific evidence, health plan reimbursement decisions, patient characteristics, and drug life cycle, each of which I discuss in detail below. Professor Rosenthal's failure to consider these factors renders her direct model unreliable and incapable of estimating the impact of Defendants' alleged false marketing activities because these factors vary over time in ways that are potentially correlated with her measures of price and marketing.

133. Professor Rosenthal's indirect model, also discussed in more detail below, suffers from similar shortcomings. By failing to consider factors that impact physicians' prescribing behavior in her model, Professor Rosenthal attributes the effects of all of these factors to Defendants' alleged misconduct. This leads her to overstate the effect of Defendants' alleged misconduct on opioid shipments and renders her conclusions unreliable.

134. There are a host of factors that can influence physician decision-making apart from marketing. One such factor that Professor Rosenthal ignores is scientific evidence. Professor Chintagunta presents evidence supporting the view that physicians' prescribing behaviors respond to scientific evidence of a drug's performance.[268] In particular, physicians follow the results of clinical trials and read different types of academic articles to keep informed on the latest developments on the drugs they prescribe. When new information becomes available, doctors adjust their prescribing behaviors accordingly. For example, in his study on the antiulcer

[267] Model C also includes additional demographic variables that could influence opioid shipments.
[268] Expert Report of Dr. Pradeep Chintagunta May 10, 2019 ("Chintagunta Report"), Section IX.A.

drug category, Azoulay (2002) shows that scientific evidence from clinical trials impacts physicians' prescribing behavior.[269] Chintagunta et al. (2009) also shows that academic publications affect physician prescription choices of Cox-2 Inhibitors, another drug category.[270] While Plaintiffs' experts allege that certain academic publications sponsored by the Marketing Defendants contain allegedly false and misleading information, Professor Chintagunta found that many academic publications on prescription opioids were not sponsored by the Teva Defendants.[271]

135. Health insurance coverage is another factor that impacts physicians' prescribing decisions, as discussed extensively above.[272] Patients are cost-sensitive with regards to co-pays, and physicians take this into consideration when making prescribing decisions. Studies also show that health insurance restrictions for one subset of patients can effect a physicians' prescribing decisions for their other patients.[273]

136. Professor Chintagunta also explains that patient age, gender, severity of the patient's illness, whether other medications are taken by the patient, and patient satisfaction can affect prescribing behaviors.[274] In addition, drug effectiveness and side effects differ from patient to patient, which also impact a physician's prescribing behavior. In fact, Professor Rosenthal herself acknowledges the importance of socio-economic and healthcare factors on the demand

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[269] Pierre Azoulay, "Do Pharmaceutical Sales Respond to Scientific Evidence?" *Journal of Economics & Management Strategy* 11, no. 4, 2002, pp. 551–594.

[270] Pradeep K. Chintagunta et al., "Information, Learning, and Drug Diffusion: The Case of Cox-2 Inhibitors," *Quantitative Marketing and Economics* 7, no. 4, 2009, pp. 399–433.

[271] Chintagunta Report Section XI.B.

[272] See Section **Error! Reference source not found.** above.

[273] Y. Richard Wang and Mark V. Pauly, "Spillover Effects of Restrictive Drug Formularies on Physician Prescribing Behavior: Evidence from Medicaid," *Journal of Economics & Management Strategy* 14, no. 3, 2005, pp. 755–773 ("Physicians who prescribe a higher proportion of Protonix to their non-Medicaid patients because of restrictive formularies also prescribe a higher proportion of Protonix to their Medicaid patients with an open formulary."); Jonathan D. Ketcham and Andrew J. Epstein, "Which Physicians are Affected Most by Medicaid Preferred Drug Lists for Statins and Antihypertensives?" *Pharmacoeconomics*, 24(3), 2006 ("Ketcham and Epstein (2006)"), pp. 27–40 at pp. 32–33 ("Physicians also reported that PDLs [*i.e.* preferred drug lists] affected drug choice for both Medicaid and non-Medicaid patients and the decision to treat new Medicaid patients at all. The average physician wrote 39% of prescriptions for Medicaid patients for drugs they viewed as inferior for the patient. Patients received no prescription an additional 4% of the time because the physician's preferred medication was not included on the PDL. Thirty percent of physicians indicated that Medicaid PDLs led to decreases in their likelihood of prescribing drugs not covered by the PDL for non-Medicaid patients.").

[274] Chintagunta Report Section IX.D.

for opioids in her indirect approach but she fails to consider any of these factors in her direct approach.[275]

137. Previous academic literature has discussed how ignoring these factors can lead to mistaken inference about the effectiveness of detailing. Datta et al. (2017) specifically emphasize that not considering patient characteristics when analyzing the effect of detailing on physician prescriptions may lead to unreliable results. In contrast to Professor Rosenthal's analysis, their analysis controlled for the market area in which physicians practice when analyzing the impact of detailing on physicians' prescribing behavior.[276] This can contribute to the prescription patterns of physicians through, for example, the profiles of the patients they treat.[277] Indeed, they found that "[t]he effect is substantially smaller than those in the literature based on aggregate information, suggesting that most of the observed relationship between physician-directed promotion and drug sales is driven by selection bias."[278]

138. Finally, Professor Rosenthal's models ignore the development and diffusion of new technology, which is an important driver of growth in healthcare spending. Diffusion is a critical part of the life cycle of a new drug. The typical life cycle of a new drug is comprised of three parts: an increase in sales during the drug's initial years on the market, a peak in sales, and a decline. Factors other than detailing can explain the diffusion and the life cycle of a new drug. For example, the efficacy of a drug and its side effects relative to incumbent products, along with insurance coverage,[279] and subsequent new entrants to the market, can all affect the drug life cycle. As Dave et al. (2012) explain, "changes in sales, price and promotion are partly governed by the drug's life cycle."[280] As a result, Professor Rosenthal's exclusion of product life cycles in her regression analysis leads to unreliable coefficients, resulting in omitted variable bias that undermine her ability to draw causal inferences about the effect of detailing on drug shipments.

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[275] Rosenthal Report, ¶ 84.
[276] The area is important to control for "disease prevalence, area demographics and economic conditions, and provider availability." See Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Behaviors: Longitudinal Evidence," *Health Economics* 26, 2017 ("Datta and Dave (2017)"), pp. 450–468 at p. 457.
[277] Datta and Dave (2017), pp. 456–457.
[278] Datta and Dave (2017), p. 450.
[279] Sheila Smith et al., "Income, Insurance, and Technology: Why Does Health Spending Outpace Economic Growth," *Health Affairs* 28 no. 5, 2009, pp. 1276–1284 at p. 1276–1279.
[280] Dave and Saffer (2012), p. 107.

139. **Exhibit 7** shows the pattern of sales from launch for Actiq and Fentora, as well as multiple other non-defendant branded opioids. Each of the opioids displayed show a similar technology diffusion trend, with sales growth, a peak, and then a decline. Cavusgil et al. (2011) show that the same trend of technology diffusion exists for drugs other than opioids. **Exhibit 8** is an exhibit from Cavusgil that shows sales after market entry for different gastrointestinal drugs, all of which exhibit the same cycle of technology diffusion.

140. Because drug life cycles have such an important effect on the diffusion of a drug and its sales, the academic literature typically controls for the life cycle of a new drug in some fashion when estimating the effect of detailing on sales. For example, Rizzo (1999) analyzes the effect of detailing on sales of antihypertensive drugs in the United States. To capture the effects of the life cycle on drug sales, he includes "a variable…that measures the number of years that the drug has been on the market and the square of this term…."[281] Similarly, Mizik et al. (2004) "empirically assess the role that two central components of pharmaceutical marketing practices (namely, detailing and sampling) have on physician prescribing behavior."[282] They include "time-specific indicator variables…[that] capture *all* effects common across physicians, which would include the diffusion pattern for the drug…."[283] Likewise, Datta et al. (2017) analyze the impact of detailing and sampling related to Famvir on the prescribing behavior of individual physicians, and include "linear and quadratic effects of the time until patent expiration, which account for the impact of Famvir's life cycle on prescription patterns."[284] In contrast to the body of academic literature that has deemed product life cycles to be an important consideration in determining the effect of detailing on sales, Professor Rosenthal fails to account for product life cycles, rendering her estimates unreliable.

141. As a result of the myriad factors discussed above, it is not surprising that sometimes physicians prescribe an approved drug as they see fit, including for conditions not listed on the

[281] John A. Rizzo, "Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs" The Journal of Law & Economics, 42 no 1, 1999 ("Rizzo (1999)"), pp. 89–116 at p. 105.
[282] Mizik and Jacobson (2004), at p. 1704.
[283] Mizik and Jacobson (2004), at p. 1709.
[284] Datta and Dave (2017), at p. 456.

label. This is usually referred to as prescribing "off-label."[285] In fact, an academic study in 2001 found that 21% of overall use of prescription drugs was off-label.[286] Some drugs commonly prescribed off-label include ciprofloxacin (Cipro), an antibiotic which is prescribed off-label 64% of the time, and dexamethasone, a corticosteroid which is prescribed off-label 79% of the time.[287] These drugs are so fundamental and common that they have made the World Health Organization's *Model List of Essential Medicines.*[288] In some contexts, off-label usage of a drug has even "become [the] predominant treatment…for a given clinical condition."[289] For example, tricyclic antidepressants are often considered to be a first-line treatment option for neuropathic pain, even though they are not indicated for this purpose.[290]

142. In sum, Professor Rosenthal ignores several factors that influence prescribers' decisions in both her direct and indirect analyses. As a result, she does not correctly estimate the impact of Defendants' marketing activities (or any alleged false marketing) on aggregate opioid shipments.

VIII. Professor Gruber Fails to Show that Opioid Shipments Cause Opioid Misuse and/or Mortality

143. Professor Gruber states in his report "that the increases in shipments of prescription opioids was a direct and substantial cause of the rapid growth in mortality from both licit and illicit opioid-related mortality in the past 20 years."[291] However, the evidence Professor Gruber relies upon for his claims are simply graphs comparing the trends in opioid-related misuse and mortality for counties which received more shipments and counties which received fewer shipments.[292] Such analyses only show that prescription opioid shipments were associated or

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[285] "Understanding Unapproved Use of Approved Drugs 'Off Label'," *U.S. Food & Drug Administration*, accessed on May 3, 2019, available at https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label.
[286] David C. Radley et al., "Off-Label Prescribing among Office-Based Physicians," *Archives of Internal Medicine* 166, 2006, pp. 1021–1026, at p. 1024.
[287] David C. Radley et al., "Off-Label Prescribing among Office-Based Physicians," *Archives of Internal Medicine* 166, 2006, pp. 1021–1026.
[288] "WHO Model List of Essential Medicines," World Health Organization Report, 20th List, https://apps.who.int/iris/bitstream/handle/10665/273826/EML-20-eng.pdf.
[289] Christopher M. Wittich et al., "Ten Common Questions (and Their Answers) about Off-Label Drug Use," *Mayo Clinic Proceedings* 87, no. 10, 2012, pp. 982–990 at p. 983.
[290] Christopher M. Wittich et al., "Ten Common Questions (and Their Answers) about Off-Label Drug Use," *Mayo Clinic Proceedings* 87, no. 10, 2012, pp. 982–990 at p. 983.
[291] Gruber Report, ¶ 72.
[292] See Gruber Report, Figures I.17, I.18, I.19, I.20.

correlated with opioid misuse/mortality—not that prescription opioid shipments *caused* higher rates of opioid-related mortality.

144. Professor Gruber does not consider the possibility that an increase in shipments of prescription opioids is simply reflective of greater demand for opioids, for reasons that are unrelated to the alleged false marketing of the defendants, and that may be related to opioid abuse and mortality.

145. In particular, the academic literature points to socioeconomic and macroeconomic factors that can influence patterns of opioid addiction. I discuss a few examples of these factors below.

A. Socioeconomic Factors

146. Drug related deaths in the U.S. have "been inexorably tracking along an exponential growth curve since at least 1979."[293] This trend predates the onset of the increase in opioid-related deaths. According to Jalal et al. (2018), the drugs responsible for the largest share of drug related deaths varied over time. According to that study, cocaine was the leading cause of drug related deaths before 2007, prescription opioids at the beginning of the 2010s, and heroin and synthetic opioids since the mid-2010s.[294] The study suggests that the overall pattern of drug abuse since the late 1970s may have a common underlying root cause by noting that, "[u]nderstanding the forces that are holding multiple subepidemics together into a smooth exponential trajectory may be important in revealing the root causes of the epidemic, and this understanding may be crucial to implementation of prevention and intervention strategies."[295]

147. A different study by Case and Deaton takes a step toward identifying the root cause of increased death rates due to drug and alcohol abuse as well as suicide.[296] The study points to an upward trend in mortality rates for non-Hispanic whites and individuals without college degrees in the U.S. since the late 1990s. According to the study, increased death rates due to drug and alcohol abuse are correlated with grim prospects on labor markets, stagnating wages, as well as declining marriage rates.

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[293] Hawre Jalal et al., "Changing Dynamics of the Drug Overdose Epidemic in the United States from 1979 through 2016," *Science* 361, no. 1184, 2018 ("Jalal et al. (2018)"), pp. 1–6 at p. 1.
[294] Jalal et al. (2018), Figure 1.A.
[295] Jalal et al. (2018), p. 5.
[296] Anne Case and Angus Deaton, "Mortality and Morbidity in the 21st Century," *Brookings Papers on Economic Activity BPEA Conference Drafts*, March 17, 2017 ("Case and Deaton (2017)"), pp. 1–59 at p. 2.

148. Neither of these studies identify the marketing or shipments of prescription opioids as the root cause of opioid abuse. Instead, the studies show that socioeconomic circumstances, which are independent of any conduct by the Teva or Actavis Generic Defendants or any other manufacturer Defendant, can and do influence opioid abuse.

B. Macroeconomic Factors

149. Several academic studies point to the relevance of short-run and long-run macroeconomic trends for individuals' likelihood to abuse drugs, and in particular, opioids. For example, Hollingsworth, Ruhm, and Simon assess the importance of short-term macroeconomic factors, such as unemployment rates, on drug related deaths and emergency department visits.[297]

150. Charles, Hurst, and Schwartz examine a more long-term macroeconomic variable, the decline of the U.S. manufacturing sector in the 2000s.[298] The study evaluates if the decline of the manufacturing sector in the U.S. (resulting in declines in hours worked, employment rates and wages) increased opioid use. The key finding is that "opioid use rose the most in precisely those places that experienced the biggest exogenous adverse shocks to manufacturing, suggesting that weak labor demand could be a factor contributing to the rising opioid epidemic in the U.S. during the 2000s."[299]

151. These studies show that short- and long-term macroeconomic factors, which are independent of any conduct by the Teva or Actavis Generic Defendants or any other manufacturer Defendant, can and do affect opioid abuse.

152. Moreover, Professor Gruber ignores other factors, including potential changes in health outcomes or in the health insurance coverage of prescription opioids that can also impact opioid prescriptions and opioid abuse.

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[297] Alex Hollingsworth et al., "Macroeconomic Conditions and Opioid Abuse," *Journal of Health Economics*, 56, 2017 ("Hollingsworth et al. (2017)"), pp. 222–233.
[298] Kerwin Kofi Charles et al., "The Transformation of Manufacturing and the Decline in U.S. Employment," NBER, May 15, 2018 ("Charles et al. (2018)").
[299] Charles et al. (2018), p. 48.

C. Professor Gruber's Attempts to Take These Factors into Account Are Inconsistent with the Academic Literature

153. The studies described above show that socioeconomic and macroeconomic factors influence opioid abuse. However, these results appear to be inconsistent with the findings of Professor Gruber. He purports to take into account "[e]conomic [c]onditions, [t]rends in [n]on-[o]pioid [d]rug [o]verdoses, and [p]opulation [d]emographics" and finds that they are "largely unrelated" to opioid mortality.[300] He even cites to the same study by Case and Deaton discussed above as evidence that economic factors are not the drivers of opioid-related trends.

154. However, Professor Gruber quotes Case and Deaton out of context to argue that medium term macroeconomic conditions do not explain opioid abuse and that "the growth in opioid mortality was driven by factors other than changes in macro-economic conditions over this period."[301] While Case and Deaton acknowledge that economic conditions are not the sole explanation, Professor Gruber fails to mention that Case and Deaton do not claim it is a result of a short-run change in the environment, but instead is a result of what they call "cumulative deprivation" which includes factors beyond medium-term macroeconomic conditions.[302] Case and Deaton "do not discount the importance of the opioid epidemic, but…regard it as having added fuel to an already bad situation, and certainly not the only cause of increasing mortality."[303] Specifically, they "attribute [these deaths] to a broad deterioration in the lives of Americans without a college degree," a deterioration that includes "the deterioration in wages for those without a BA…the decline in labor force participation [and] the decline in marriage rates," among other trends, of which "economic decline is part."[304]

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[300] Gruber Report, ¶ 100.
[301] Gruber Report, ¶ 103.
[302] Case and Deaton (2017), p. 29.
[303] Anne Case and Angus Deaton, "Deaths of Despair Redux: A Response to Christopher Ruhm," January 8, 2018 ("Case and Deaton (2018)"), p. 3.
[304] Case and Deaton (2018), p. 2.

IX. Professor Gruber Does Not Show That the Defendants' Allegedly False Marketing Caused Illicit Opioid Use, and He Does Not Properly Take into Account Other Factors that Contributed to the Increase in Illicit Opioid Use

155. Professor Gruber makes several unsubstantiated and misleading claims regarding the linkage between prescription opioid shipments and illicit opioids and how Defendants' conduct "result[ed]" in the increased illicit opioid mortality and misuse, including:

- "There is a direct, causal relationship between defendants' shipments of prescription opioids and the misuse of and mortality from illicit opioids, including heroin and fentanyl, which accelerated rapidly after 2010 ."[305]
- "[M]y analysis demonstrates that the illicit opioid crisis that has emerged since that time is directly related to the defendants' earlier shipments of licit prescription opioids."[306]
- "Increases in the demand for illicit opioids, and the associated increases in mortality, would not have occurred in the absence of the enormous increase in prescription opioid shipments resulting from defendants' misconduct, which effectively created a stock of individuals susceptible to illicit opioid use and abuse."[307]
- "[T]he illicit opioid crisis is a direct result of defendants' misconduct."[308]

156. These unsubstantiated claims are then repeated by Plaintiff's other experts as support for the improper inclusion of harms or damages related to the illicit opioid mortality and misuse. For example, Professor Cutler states that, "as also concluded by Professor Gruber, the increase in the demand for illicit opioids, and the associated increases in mortality, would not have occurred in the absence of the enormous increase in prescription opioid shipments resulting from defendants' misconduct, which effectively created a stock of individuals susceptible to illicit opioid use and abuse."[309]

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[305] Gruber Report, ¶ 16.
[306] Gruber Report, ¶ 12.
[307] Gruber Report, ¶ 16.
[308] Gruber Report, ¶ 89.
[309] Cutler Report, ¶ 53.

157. Professor Gruber claims that prescription opioids are the "predominant gateway to heroin use," and discusses the trends in heroin usage as well as the emergence of fentanyl.[310] However, he does not account for the fact that, as discussed above, there are several factors that trigger substance abuse issues (apart from marketing) and individuals who abuse illicit opioids may have done so even absent the Defendant's conduct. Furthermore, Professor Gruber conflates individuals who transition towards illicit opioid use due to Defendants' allegedly false marketing activities with those who use illicit opioids for reasons wholly unrelated to these activities, such as those users who acquired their prescription opioids illegally.

158. Below, I discuss why Professor Gruber's conclusions are flawed, misleading, and unreliable. Namely, he fails to show how the Teva Defendants' allegedly false marketing activities caused illicit opioid use, and does not properly take into account factors he himself admits contributed to illicit opioid mortality and misuse.

A. Professor Gruber Fails to Show Any Causal Link between Defendants' Alleged False Marketing Conduct and Illicit Opioid Use

159. Professor Gruber describes the rise of illicit opioid mortality and misuse but does not acknowledge that those who misuse illicit opioids (whether heroin or fentanyl) may do so for a variety of reasons unrelated to any of the actions of the Defendants. Rather he asserts the "illicit opioid crisis is a direct result of defendants' misconduct."[311] This is problematic for several reasons.

160. First, Professor Gruber appears to discount the possibility of illicit opioid users who never used prescription opioids at all. However, the studies he cites in his report provide evidence that this happens. For example, Professor Gruber notes that Cicero et al. found that roughly 65 percent of opioid users who initiated opioid abuse between 2010 and 2013 initiated opioid use with prescription opioids.[312] Putting aside the merits of this study, this implies that more than a third of these opioid users did not begin with prescription opioids and as such, could not have been affected by Defendants' marketing conduct.

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[310] Gruber Report, ¶ 89.
[311] Gruber Report, ¶ 89.
[312] Gruber Report, ¶ 92.

161. Second, Professor Gruber fails to acknowledge the difference between users of medically prescribed opioids and users who illegally obtain prescription opioids (whether through pill mills, street dealers, or other means). The 2017 National Survey on Drug Use and Health found that nearly two-thirds (63.9 percent) of the people who misused prescription pain relievers did not obtain their pain relievers legally from a doctor for their most recent misuse.[313] Similarly, a 2011 study by Cicero et al. regarding prescription opioid diversion reported that "[j]ust 13.8% of respondents reported obtaining their abused opioids through legitimate medical sources (by doctor shopping or from their regular doctor)."[314] Use of prescription opioids without a medical prescription must be unrelated to Defendants' marketing conduct. Therefore, if the majority of illicit opioid users who initiated opioid use with prescription opioids obtained those prescription opioids without a proper medical prescription, then the consequences of that illicit opioid mortality and misuse must not be attributed to Defendant's marketing conduct.

162. Professor Gruber cites five epidemiological studies in support of his assertion linking prescription opioids to heroin use—however, all of these studies measure the link for either individuals with *nonmedical* opioid use, or with opioid use disorder.[315] For instance, Muhuri, et al. "finds a strong association between prior *nonmedical* use of pain relievers and the subsequent past year initiation of heroin use" (emphasis added).[316] Some studies indicate that when individuals use opioid for medical reasons, they are unlikely to become addicted. For example, a 2010 analysis in the Cochrane Database of Systematic Reviews found that less than 1 percent of patients taking opioids for chronic pain experienced addiction or abuse.[317] Similarly, a review by

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[313] "Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health," Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services Publication No. SMA 18-5068, September 2018, p. 22.

[314] Theodore J. Cicero et al., "Multiple Determinants of Specific Modes of Prescription Opioid Diversion," *Journal of Drug Issues* 41, no. 2, 2011, pp. 283–304.

[315] Gruber Report, Table I.1.

[316] Pradip K. Muhuri et al., "Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States," *CBHSQ Data Review*, August 2013, p. 14.

[317] Meredith Noble et al., "Long-term Opioid Management for Chronic Noncancer Pain," *Cochrane Database of Systematic Reviews*, Issue 1, 2010, pp. 1–69 at p. 8. Noble et al. review a number of studies which separately report on the number of cases of opioid addiction observed. One study, for example, reports addiction using "criteria for opioid abuse and/or addiction as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)."

Vowles et al. of 38 studies of patients with opioid prescriptions for chronic non-cancer pain found that 8 to 12 percent developed an addiction.[318]

163. I also note that several of the epidemiology studies Professor Gruber cites to, such as Jones (2013), are studies that only focus on heroin users. That is, these studies do not consider non-heroin users but are "selecting on the outcome" (i.e., heroin users). This is widely known as a flawed research design and cannot be used to draw any conclusions on causality between prescription opioid usage and heroin usage.

164. While Professor Gruber admitted in deposition that there are many paths that can lead to someone becoming a heroin user, "studying other pathways to heroin use isn't something that [he] did in this case."[319] By ignoring the different pathways in which individuals become addicted to illicit opioids, Professor Gruber cannot attribute illicit opioid mortality and misuse to the Defendants' alleged unlawful marketing conduct.

B. Professor Gruber Lists Multiple Factors that Contributed to Illicit Opioid Use post-2010, yet Implies that Defendants Are Primarily Responsible for It

165. While Professor Gruber asserts that the "illicit opioid crisis is a direct result of defendants' misconduct," he concedes elsewhere in his report that there are "several factors contributing to the shift of demand from prescription opioids to illicit opioids."[320] Under his own admission, the shift to illicit opioids could be attributed to many factors besides any Defendants' conduct. However, Professor Gruber does not provide analysis to determine how much of this shift is caused by any single factor or reason. Instead, he finds that Defendants are primarily responsible.

166. In his report, Professor Gruber gives the following factors, among others, that led to illicit drug use:[321]

- "powder heroin proved to be a closer substitute for prescription opioids"
- "heroin was more readily available and less expensive"

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[318] Kevin E. Vowles et al., "Rates of Opioid Misuse, Abuse, and Addiction in Chronic Pain: A Systematic Review and Data Synthesis," *PAIN* 156, no. 4, 2015, pp. 569–576 at p. 574.
[319] Deposition of Jonathan Gruber, April 25, 2019, ("Gruber Deposition"), 261:5–14.
[320] Gruber Report, ¶¶ 51, 89.
[321] Gruber Report, ¶¶ 46, 47, 54, 55, 62, 67, 93.

- fentanyl "entered the illicit drug market through illegal imports, mainly from China and Mexico"
- "fentanyl is often mixed with heroin and other drugs to lower the cost to drug dealers and to increase the high to users"
- "(unobservable) local supply conditions"
- "criminal actions and litigation"
- "increased enforcement actions by DEA and DOJ"
- "the growth of state PDMP laws"
- "increased awareness of addiction risks"
- "pill-mill legislation"
- "Purdue Pharmaceuticals launched its abuse deterrent formulation of OxyContin"

167. Each factor above is not an action of the Teva or Actavis Generic Defendants, the Mallinckrodt Defendants, or the Janssen Defendants. Many of these factors are actions by government entities designed to restrict the supply of prescription opioids, which in turn "raised the relative costs of using prescription opioids" and were meant to help reduce opioid abuse.[322] As I discussed earlier in this report, government entities could have taken many of these actions sooner than they did, or could have implemented stricter actions which may have reduced access to prescription opioids and decreased the "stock of individuals susceptible to illicit opioid use and abuse."[323]

168. However, other factors, such as the price of heroin and illegal fentanyl imports, relate to the supply of illicit drugs. For example, Professor Gruber explains how drug dealers substituted fentanyl for heroin to earn larger margins and increase the sales of heroin and how fentanyl was

[322] Gruber Report, ¶ 51.

[323] Gruber Report, ¶ 16. I also note that Professor Gruber's assertion that the "enormous shipments" of prescribed opioids resulted in a "stock of individuals susceptible to illicit opioid use and abuse" is unsubstantiated. Professor Gruber does not quantify or provide any evidence of this "stock of individuals" nor does he explain why there was no substitution to heroin prior to 2010. Professor Gruber appears to assume that illicit and licit opioids were complements prior to 2010 but substitutes afterwards.

illegally imported from China and Mexico.[324] Similarly, the National Drug Intelligence Center in a national drug threat assessment report found that "the increase in heroin availability has resulted in an increase in heroin-related overdoses"; this increase is due to factors such as "the eastward expansion of Mexican trafficking organizations," which is unrelated to Defendants.[325] Professor Gruber does not explain why any mortality or misuse arising from such actions should be attributed to Defendants.

169. A large portion of Professor Gruber's discussion of the shift towards illicit opioids also focuses specifically on the reformulation of OxyContin, which "was one of many other causes that led to increased illicit heroin use" as it made "abusing OxyContin more difficult."[326] I note that Professor Gruber is unclear as to whether the reformulation was effective or not as he also states in his report that "abuse deterrent formulations did not eliminate the risk of addiction or abuse" and cites to an article about how OxyContin could still be abused orally.[327] Nevertheless, in his deposition, he stated that he "would view this as the reformulation causing the inflection" in illicit opioid use.[328] In his report, Professor Gruber also cites to two papers with the following findings:

- "Our results imply that the recent heroin epidemic is largely due to the reformulation of OxyContin."[329]
- "We attribute the recent quadrupling of heroin death rates to the August, 2010 reformulation of an oft-abused prescription opioid, OxyContin."[330]

170. These papers claim that the increase in heroin mortality is tied to the reformulation of OxyContin. This is unrelated to the conduct of the Teva and Actavis Defendants (or the

[324] Gruber Report, ¶¶ 55, 58.
[325] "National Drug Threat Assessment 2011," U.S. Department of Justice National Drug Intelligence Center Product No. 2011-Q0317-001, August 2011, pp. 27–28.
[326] Gruber Report, ¶¶ 46–48.
[327] Gruber Report, ¶ 51 and fn 64.
[328] Gruber Deposition, 435:20–436:16.
[329] Abby Alpert et al., "Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids," *American Economic Journal: Economic Policy* 10, no. 4, 2018, pp. 1–35.
[330] William N. Evans et al., "How the Reformulation of Oxycontin Ignited the Heroin Epidemic," *The Review of Economics and Statistics* 101, no. 1, 2019, pp. 1–15.

Mallinckrodt and Janssen Defendants), and Professor Gruber does not explain why Teva should be responsible for any impact of the reformulation.

171. Professor Gruber makes numerous assertions and provides evidence that use of prescription opioids and illicit use of heroin and fentanyl are substitutes. In fact, his claims about substitutability between the two are required for the logic behind his unsubstantiated claims that the "enormous increase in prescription opioid shipments" resulted in a "stock of individuals susceptible to illicit opioid use and abuse."[331] Professor Gruber does not quantify or provide any evidence of this "stock of individuals" nor does he explain why there was no substitution to heroin prior to 2010. Professor Gruber also provides no analysis of the extent to which, prior to 2010, individuals who would have otherwise used illicit opioids used prescription opioids. This seems relevant to appropriately quantify the impact of prescription opioids on Plaintiffs.

172. Furthermore, I understand that when using Professor Cutler's direct modeling framework, Professor Nicholson does not find a statistically significant relationship between average prescription opioid shipments (over 1997-2010) and the change in illicit opioid mortality rates after 2008.[332] As I describe elsewhere, to the extent that such a "stock of individuals susceptible to illicit opioid use and abuse" existed in 2010, Professor Gruber makes no attempt to determine whether such individuals are susceptible due to the alleged actions of the Marketing Defendants or due to other reasons. In fact, Professor Gruber provides no explanation of any link between the alleged actions of the Marketing Defendants and "illicit opioid use and abuse," whether through diversion of prescription drugs or through use of illegal drugs.[333]

173. To summarize, Professor Gruber claims that all of these factors contributed to illicit opioid use, but simultaneously places the blame primarily on the "defendants' shipments of prescription opioids."[334] In his deposition, Professor Gruber confirmed that he had not "apportioned how each of those causal factors contributed to illicit opioid use"[335]; that is, he did not attempt to ascertain what portion of the illicit opioid use is due to Defendants' Alleged Conduct, and instead placed the blame on Defendants for factors unrelated to Defendants'

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[331] Gruber Report, ¶ 16.
[332] Expert Report of Sean Nicholson, Ph. D., Section 7.7.2.2.
[333] Gruber Report, ¶ 16.
[334] Gruber Report, ¶ 63.
[335] Gruber Deposition, 64:4–64:8.

alleged actions. As such, his claims that Defendants' conduct "result[ed]" in the illicit opioid mortality and misuse are misleading.[336]

X. Professor Gruber's Analysis Claiming that Shipments of Opioid Prescriptions Are Associated with Higher Crime Is Flawed

174. Professor Gruber claims to perform a brief review of the linkage between prescription opioids shipments and crime and then concludes that "shipments of prescription opioids are also associated with higher crime."[337] Professor Gruber also speculates that "opioid misuse is also likely to lead to increases in property crimes (e.g. theft) or violent crimes (e.g. assault or robbery). For example, people using opioids may commit property or violent crimes to finance opioid addiction or because opioid addiction leads people to behavior that they would not otherwise engage in."[338] However, no evidence (anecdotal or otherwise) is provided to support this hypothesis. In fact, it is important to note that Professor Gruber's analysis merely purports to show association, not causation, and it is also possible that higher crime might be the cause of the higher volumes of prescription opioids.[339]

175. Professor Gruber's finding may be an instance of omitted variable bias. For example, it could be that shipments are correlated with causal factors such as unemployment rates, income inequality, and education rates. Not controlling for any of these factors renders Professor Gruber's analysis simplistic, possibly even misleading, and unreliable.

176. Some evidence of the relationship between crime and various socioeconomic factors such as unemployment, urbanization, income inequality, and poverty is available in the academic literature. For example,

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[336] Gruber Report, ¶ 89.
[337] Gruber Report, ¶ 19.
[338] Gruber Report, ¶ 109.
[339] For example, this could be because higher crime rates allow for higher diversion rates of opioids, leading to increased shipments, or because areas with higher crime have medical needs that call for higher shipments of prescription opioids.

- Raphael and Winter-Ebmer in their study on the effect of unemployment on crime find "significantly positive effects of unemployment on property crime."[340]
- Glaeser and Sacerdote find in their paper that crime rates are higher in cities than in rural areas because of factors including lower probability of arrest and recognition, and the presence of more female-headed households.[341]
- Fajnzylber et al.'s study that investigates the causality between income inequality and violent crime finds that income inequality has a significant and positive effect on violent crime.[342]
- Lochner and Moretti's study on the effects of education on incarceration find that high school education significantly reduces criminal activity, with the biggest impacts associated with assault, murder, and motor vehicle theft.[343]

177. Professor Gruber considered none of these factors.

XI. Professor Rosenthal's Direct Approach Suffers from Multiple Flaws, Is Unreliable, and Is Not Capable of Establishing a Causal Relationship between Defendants' Alleged Promotion of Opioids and Opioid Shipments. It Also Cannot Establish a Causal Relationship between Teva and Actavis Generic Defendants' Alleged Promotion and Opioid Shipments

178. Professor Rosenthal purports to "quantify directly the causal relationship between promotion and sales" by using what she calls "the direct approach."[344] In this section I first give an overview of her methodology and then I explain why it is not capable of establishing a causal relationship between the Defendants' promotion of opioids and opioid shipments.

179. To illustrate the unreliability of the direct approach in drawing causal inferences about the effects of promotion, I first rely on well-established model validation techniques based on

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[340] Steven Raphael and Rudolf Winter-Ebmer, "Identifying the Effect of Unemployment on Crime," *The Journal of Law and Economics* 44, no. 1, 2001, pp. 259–283 at p. 259.
[341] Edward L. Glaeser and Bruce Sacerdote, "Why Is There More Crime in Cities?" *Journal of Political Economy* 107, no. S6, 1999, pp. S225-S258 at p. S225.
[342] Pablo Fajnzylber et al., "Inequality and Violent Crime," *The Journal of Law and Economics* 45, no. 1, 2002, pp. 1-40.
[343] Lance Lochner and Enrico Moretti, "The Effect of Education on Crime: Evidence from Prison Inmates, Arrests, and Self-Reports," NBER Working Paper No. 8605, November 2001.
[344] Rosenthal Report, ¶ 10.

"placebo tests." Specifically, her logic, model, and interpretation can be used to show the following: 1) that random numbers cause opioid shipments to virtually the same extent as opioid detailing; 2) that opioid detailing has a causal effect on the price of gold; and 3) that virtually all of the opioid shipments for the period 2003–2018 were caused by detailing prior to March 2002 alone. These spurious relationships demonstrate the unreliability and lack of usefulness of Professor Rosenthal's direct approach to establish a causal relationship between Defendants' alleged promotion of opioids and opioid shipments.

180. An important flaw in Professor Rosenthal's model is her use of a negative depreciation rate. After discussing the problematic nature of such a depreciation rate, I show that the use of depreciation rates that are more consistent with the academic literature yields results that directly contradict Professor Rosenthal's conclusions.

181. Finally, I describe a variety of other methodological flaws with the direct approach.

A. Overview of Professor Rosenthal's Direct Approach

182. In the econometric approach she terms the "direct approach," Professor Rosenthal attempts to quantify the effect of promotion on total shipments of opioids. The specific technique that she uses is a time series regression analysis and she asserts that such a technique captures "a dynamic causal relationship."[345]

183. The unit of observation in this regression is a month, aggregated across the entire U.S and across all opioid drugs.[346] That is, the dependent variable used in this regression analysis is the number of morphine milligram equivalents ("MMEs") of all drugs (across all manufacturers) sold in the entire U.S. in a given month.[347] In other words, Professor Rosenthal aggregates opioid drugs and geographies, and does not conduct the analysis at the manufacturer, drug, physician, or county level. The sample period ranges from January 1993–May 2018.[348]

184. Professor Rosenthal includes just two explanatory variables in her preferred specification: a measure of marketing based on the number of detailing contacts (i.e., the number of visits by

[345] Rosenthal Report, ¶ 58.
[346] Rosenthal Report, ¶ 58.
[347] Rosenthal Report, ¶ 59.
[348] Rosenthal Report, Table 1.

sales representatives to physicians' offices) and a price index.[349] The monthly number of detailing contacts ("flow") is not the variable used in the regression, however. Professor Rosenthal instead uses the "detailing stock," which is equal to the detailing flow in that month plus the detailing stock in the previous month discounted by δ, the depreciation rate.[350]

185. Professor Rosenthal estimates three different models.[351] Model A is a regression based on the detailing stock and the price index, as described above. The regression jointly estimates the coefficients for the explanatory variables and the value of δ.[352] According to Professor Rosenthal, she develops a second model (Model B) because of alleged changes in prescribing attitudes and guidelines during the period she uses to conduct the regression analysis.[353] She identifies three sub-periods—one until March 2002, another through July 2010, and a third starting in August 2010—but does not use the same specification for each one, and provides no explanation for this inconsistency.[354] She uses the same intercept and coefficient on the price index throughout the period of her regression. The coefficient on the stock of marketing during the first sub-period is β_1; this coefficient during the second sub-period is β_2. For the third sub-period, from August 2010 onwards, which covers the decline in opioids shipments, Professor Rosenthal changes her approach: the coefficient on the stock of marketing changes every month instead of being the same during this sub-period. To do so, she introduces a new parameter, β_3, which represents the amount by which the coefficient on the stock of marketing decreases every month. For example, August 2010 is the first month of the third sub-period and the coefficient for this month is $\beta_2 + \beta_3 * 1$, or approximately 1103.[355] Similarly, the coefficient for September 2010–the second month in the third sub-period–is $\beta_2 + \beta_3 * 2$ or approximately 1095. The coefficient for May 2018, the 94th month in the third sub-period, is $\beta_2 + \beta_3 * 94$ or approximately 362.[356] In essence, the coefficient on the stock of marketing linearly decreases over time during the third sub-period. She also develops a third model, Model C, but concludes

[349] Rosenthal Report, ¶ 60.
[350] Rosenthal Report, ¶ 62.
[351] Rosenthal Report, Table 1.
[352] Rosenthal Report, Table 1.
[353] Rosenthal Report, ¶ 71.
[354] Rosenthal Report, ¶ 71.
[355] Author's own calculations, based on code that generates results in Rosenthal Report, Table 1.
[356] The result differs from 1111-8*94 because 1,111 and 8 are rounded.

that this model "barely improves upon the adjusted R-squared in Model B and the main results concerning promotion and price are little changed."[357]

186. Professor Rosenthal concludes that "Model B is a fair, accurate and econometrically sound method by which to estimate the relationship of the Defendants' detailing of opioids on the sales of prescription opioids over the time period 1993 to 2018."[358]

187. Based on this Model B, Professor Rosenthal claims to calculate the percentage of MMEs attributable to the alleged unlawful promotion. To do so, she purports to calculate but-for MMEs (the number of MMEs that would have been shipped absent the alleged misconduct) by assuming that 1) "all promotion by the manufacturer Defendants from 1995 to the present was unlawful," and 2) in the but-for world, Defendants would not have promoted opioids at all starting in 1995.[359] Using these assumptions and her estimates of Model B, she calculates the difference between the predicted actual MMEs (i.e., the prediction of actual MMEs using the coefficients of Model B) less the predicted but-for MMEs (adjusting the detailing flow for Defendants based on the methodology previously described) and divides this difference by the predicted actual MMEs, which represents her estimate of the percentage of MMEs attributable to the alleged unlawful promotion in any given month.[360] She then averages these monthly percentages within each year and across the full period of her regression.[361]

B. Professor Rosenthal's Model B Cannot Provide Any Insight Into the Relationship between Opioid Shipments and Opioid Detailing, and Cannot Be Used to Establish that Detailing Causes Shipments

188. Professor Rosenthal asserts that her econometric analysis serves the purpose of showing "a causal relationship between the Defendants' promotion and prescriptions of opioids."[362] She asserts that "[t]he predictive power of Model B is shown to be quite good with an R-square [sic] of 0.9937, thus explaining over 99% of the variation in MME sales"[363] and, as mentioned above,

[357] Rosenthal Report, ¶ 73.
[358] Rosenthal Report, ¶ 74.
[359] Rosenthal Report, ¶ 75.
[360] Rosenthal Report, ¶ 75.
[361] Rosenthal Report, Table 2.
[362] Rosenthal Report, ¶ 64.
[363] Rosenthal Report, ¶ 72.

that Model B is a "sound method by which to estimate the relationship of the Defendants' detailing of opioids on the sales of prescription opioids over the time period 1993 to 2018."[364]

189. However, Model B cannot show any such causal relationship. Rather, the sources of the artificial and positive correlation between opioid shipments and the detailing stock are 1) the negative δ, and 2) the coefficient on marketing that is linearly decreasing over time during the third sub-period, when opioid shipments are decreasing. As shown in Figure 4 of the Rosenthal report, a negative δ creates an upward trending curve for the detailing stock, which allows for a strong correlation with the upward trending part of the opioid shipments curve. This is because, when δ is negative, the effect of past detailing on opioid shipments grows over time. Moreover, Professor Rosenthal's inclusion of a coefficient on marketing that is linearly decreasing over time during the third sub-period artificially creates a positive correlation between the detailing stock and opioid shipments, even during a period when opioid shipments are experiencing a decline, but when the stock of detailing is still rising.

190. I demonstrate the inability of Professor Rosenthal's model to establish a causal relationship between the stock of detailing and opioid shipments using three validation tests. These test whether a model is properly specified and whether the potential insights from the model are reliable.[365] A sound model should not show a relationship between a dependent variable and an explanatory variable with which it cannot possibly have a causal relationship. For example, the returns on the S&P 500 cannot cause temperature fluctuations in Chicago. According to Athey and Imbens, "[t]he implication of rejection here is that it is possible the original analysis was not credible at all."[366]

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[364] Rosenthal Report, ¶ 74.

[365] For example, in an analysis featuring a placebo outcome, "the researcher replicates the primary analysis with the outcome replaced by a pseudo outcome that is known not to be affected by the treatment. Thus, the true value of the estimand for this pseudo-outcome is zero, and the goal of the supplementary analysis is to assess whether the adjustment methods employed in the primary analysis, when applied to the pseudo-outcome, lead to estimates that are close to zero." See Susan Athey and Guido W. Imbens, "The State of Applied Econometrics: Causality and Policy Evaluation," *Journal of Economic Perspectives* 31, no. 2, 2017, pp. 3–32 at p. 17. Bertrand et al. pursue precisely the opposite approach: They consider placebo "causes"—placebo "laws" that are assigned to states at random—that could not possibly cause any economic outcomes in these states, since they are not real. Then they study the "effect" of these laws on female wages using various methods of standard error computation to determine which methods are appropriate. Marianne Bertrand et al., "How Much Should We Trust Differences-In-Differences Estimates?" *Quarterly Journal of Economics* 119, no. 1, 2004, pp. 249–275.

[366] Susan Athey and Guido W. Imbens, "The State of Applied Econometrics: Causality and Policy Evaluation," *Journal of Economic Perspectives* 31, no. 2, 2017, pp. 3–32 at p. 17.

191. Professor Rosenthal asserts that her Model B establishes that detailing causes opioid shipments. If Professor Rosenthal's Model B were reliable for inferring causality, then it should not show that 1) a variable that is facially unrelated to opioid shipments causes opioid shipments; 2) the change in a variable that is facially unrelated to detailing was causally affected by detailing; and 3) opioid shipments for the period 1995–2018 are fully explained by the detailing that occurred before March 2002. I implemented these three types of tests and found that Model B fails all of them.

192. Specifically, with respect to the first test, I used a sequence of random numbers in place of the detailing data used by Professor Rosenthal. In other words, for every month in the period covered by Model B, I randomly generated a number between 0 and 100 that I multiplied by 1,000.[367] Then, I estimated Professor Rosenthal's Model B—all coefficients, the depreciation rate, and the structural break points—using precisely her methodology, but replacing the detailing data with these random numbers. I collected the R-squared statistics, as well as the coefficients and their respective statistical significance. I repeated this procedure 1,000 times.

193. The results, presented in **Exhibits 9 and 10,** show why Professor Rosenthal's model cannot be used to establish a relationship between marketing and opioid shipments. For the one thousand iterations of the procedure previously mentioned, the lowest R-squared is 0.9927 and the highest R-squared is 0.9942—almost identical to the R-squared statistic for Professor Rosenthal's Model B. Also, the coefficients on all of the variables, including opioid prices and the randomly generated variable, always have the same signs as those in Model B. In addition, the coefficients associated with the stock of random numbers are always statistically significant at the 95% confidence level and the coefficients associated with the price index are statistically significant at this confidence level 98% of the time. That is, my randomly generated variable, when turned into a stock using Professor Rosenthal's methodology and following Professor Rosenthal's model and logic, "caused" opioid shipments. It is important to note that for these one thousand iterations, I always find a negative depreciation rate and a negative β_3, which is the parameter used to adjust on a monthly basis the coefficient on the stock of marketing during the third sub-period—just as Professor Rosenthal does using the true detailing data.

[367] The multiplication by one thousand is used to have a magnitude comparable to the magnitude of the monthly flow in the data. The random numbers uniformly distributed between 0 and 100, i.i.d.

194. The conclusion from this exercise is clear. By allowing the depreciation rate to take negative values and by using a coefficient on marketing that is linearly decreasing over time during the third sub-period, Professor Rosenthal's Model B creates an artificial positive correlation between opioid shipments and ***any*** type of positive data, whether a truly random data as I have used or a measure of actual detailing as she has used. In other words, Professor Rosenthal's model essentially guarantees that she will find a positive association between the stock of detailing and an increase in opioid shipments even if there is no causal relationship, as in the case of my 1,000 sets of random numbers.

195. As I will explain in the next section, a negative depreciation rate is illogical and inconsistent with the academic literature,[368] despite Professor Rosenthal's attempt to justify it. In addition, Professor Rosenthal claims that using a coefficient on marketing that is linearly decreasing over time during the third sub-period should capture the "secular decrease in promotional effectiveness,"[369] which is in turn the result of "countervailing factors such as the introduction of mandatory prescription drug monitoring programs and new treatment guidelines,"[370] but she does not provide any academic support or evidence to show that such a linear trend is the proper way to model these countervailing effects.

196. I conducted a second test to further illustrate the inability of Model B to establish a causal relationship between marketing and opioid shipments. In this test I replaced the opioid shipments variable—the dependent variable—with the price of gold.[371] I then estimated Professor Rosenthal's model using her explanatory variables, including her detailing stock variable. **Exhibits 11 and 12** present the results. I found an R-squared of 94.94% which is nearly as high as the R-squared for Professor Rosenthal's Model B. The coefficients are statistically significant at the 99% confidence level and their signs match those presented in Table 1 of the Rosenthal report. Thus, even though detailing for opioids is unrelated to the price

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[368] Even Professor Rosenthal admits in her deposition that she is not aware of any academic literature supporting the use of a negative depreciation rate: ("Q. As you sit here right now, do you know of any literature, whether related to nonaddictive or addictive products, that has a negative depreciation rate? A. I cannot point to any study, no.") Deposition of Meredith B. Rosenthal, May 4–5, 2019 ("Rosenthal Deposition"), 259:25–260:6.

[369] Rosenthal Report, ¶ 71.

[370] Rosenthal Report, ¶ 65.

[371] ICE Benchmark Administration Limited (IBA), Gold Fixing Price 3:00 P.M. (London time) in London Bullion Market, based in U.S. Dollars [GOLDPMGBD228NLBM], retrieved from FRED, Federal Reserve Bank of St. Louis; https://fred.stlouisfed.org/series/GOLDPMGBD228NLBM, May 6, 2019.

of gold, using Professor Rosenthal's model and logic we would conclude that a causal relationship exists between the two. If we reject that conclusion, we must reject Rosenthal's model and/or its usefulness for drawing causal inferences.

197. I conducted a third test, where I used Professor Rosenthal's methodology to calculate detailing stock assuming that no detailing happened after February 2002 but otherwise make no changes to Model B. As shown in **Exhibits 13 and 14**, using this adjusted explanatory variable, Model B provides an R-squared of 99.36% and all the coefficients are statistically significant at the 99% confidence level with the same signs as those shown in Table 1 of the Rosenthal Report. The implication is that, following Professor Rosenthal's logic, detailing prior to March 2002 caused opioid shipments for the period 1995–2018.

198. These three analyses demonstrate that Professor Rosenthal's Model B is flawed and unreliable for establishing any causal relationship between opioid detailing visits and opioid shipments.

C. The Negative Depreciation Rate Estimated by Professor Rosenthal Is Evidence That Her Model Is Unreliable

199. Professor Rosenthal estimates a negative δ for Model B.[372] This means that shipments in the current period are impacted more by past detailing than by current detailing for a given estimated coefficient of the stock of detailing on shipments, $\beta, \beta_1, \beta_2,$ and β_3. Setting aside for the moment the numerous limitations of the model noted elsewhere, there are two possible interpretations of Professor Rosenthal's Model B: (a) one in which the stock of detailing represents physicians' recollection of current and past detailing visits; and (b) one in which the model is the simplification of a more complicated model, possibly involving addiction as stated by Professor Rosenthal. I discuss the implications of these two interpretations one at a time; each set of implications is deeply problematic for Professor Rosenthal's conclusions.

200. If Professor Rosenthal's model is to be taken literally, then a negative depreciation rate is contradicted by academic literature and common sense. Numerous academic articles in the field of marketing (including the marketing of pharmaceuticals) consider or estimate a depreciation

[372] Rosenthal Report, Table 1.

rate that is between zero and one.[373] Professor Rosenthal provides no academic support for her use of a negative deprecation rate. Common sense also requires a positive depreciation rate. The intuition behind a positive depreciation rate is that a physician may remember a detailing visit that occurred several months ago, but will remember it less well than a detailing visit that occurred more recently.[374] On the other hand, the implication of a negative deprecation rate—that a physician will remember a detailing visit in the more distant past better than one in the more recent past—is illogical.

201. Professor Rosenthal anticipates these criticisms and acknowledges that a negative depreciation rate is "at odds with the usual marketing literature."[375] However, rather than evaluating the implications for her model, she attempts to rationalize this result by stating "it is perfectly consistent with an addictive product like opioids."[376] In her expert report, she does not elaborate on this assertion and does not explain the logic behind it.[377] She simply refers to a statement in another expert report submitted by Plaintiff without explaining how this statement justifies a negative depreciation rate: "[B]ecause prescription opioids may result in dependence, and/or addiction, the overall 'demand' for opioids is distorted by pharmaceutical marketing aimed at increasing the use of these drugs…some patients who use opioids require and/or seek more opioids over time."[378]

202. This explanation suggests the second interpretation of her model: the simplification of a model involving addiction. However, this interpretation is problematic for two distinct reasons.

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[373] Rizzo (1999), p. 96; Marc Nerlove and Kenneth J. Arrow, "Optimal Advertising Policy under Dynamic Conditions," *Economica* 29, no. 114, 1962 ("Nerlove and Arrow (1962)"), pp. 129–142 at pp. 130–131; Jean-Pierre Davina C. Ling et al., "Deregulation Direct-to-Consumer Marketing of Prescription Drugs: Effects on Prescription and Over-the-Counter Product Sales," *Journal of Law and Economics* 45, 2002, pp. 691–723 at pp. 710–711; Julie M. Donohue and Ernst R. Berndt, "Effects of Direct-to-Consumer Advertising on Medication Choice: The Case of Antidepressants," *Journal of Public Policy & Marketing* 23, no. 2, 2004, pp. 115–127 at p. 119; Sridhar Narayanan et al., "Temporal Differences in the Role of Marketing Communication in New Product Categories," *Journal of Marketing Research* 42, no. 3, 2005, pp. 278–290 at pp. 279, 284.

[374] Nerlove and Arrow (1962), p. 130.

[375] Rosenthal Report, ¶ 72.

[376] Rosenthal Report, ¶ 72.

[377] In her deposition, Professor Rosenthal explains: "As you know, my model is estimating the relationship between promotion and sales for an addictive good, and so what we're saying is let's say promotion caused them – the physician to write a hundred MMEs in a prescription today, as the patient gets more tolerant, not only do they continue writing that prescription because the patient comes back, but also the dose goes up. So that is really what the negative depreciation rate is about here." Rosenthal Deposition, 249:16–250:1. It does not address the issues that I detail in this section.

[378] Rosenthal Report, fn 103.

203. First, Professor Rosenthal does not show that such a model, with plausible parameters, is equivalent to the model she estimates. In fact, she does not propose or estimate such a model at all. If this is the sort of model Professor Rosenthal had in mind, then she should have proposed and estimated such a model, following best practices in the peer-reviewed economics literature on addiction. In this literature on addiction, the depreciation rate reflects the influence of past consumption (rather than promotion) on present consumption. A negative depreciation rate is inconsistent with this literature as well.[379]

204. Second, if Professor Rosenthal in fact estimated the simplification of a model involving addiction, then it is not the case that "[t]he effectiveness of detailing is reflected in the parameters $\beta, \beta_1, \beta_2,$ and β_3."[380] Instead, these coefficients represent merely (possibly quite complicated) functions of a variety of factors that are associated with opioid shipments. Thus, if this is the correct interpretation of Professor Rosenthal's analysis, she *has failed to demonstrate that marketing has any statistically or economically significant effect on shipments at all*, because she has not estimated such a parameter, and the parameters that she has estimated cannot isolate the effects of marketing.

205. In summary, a negative δ as estimated by Professor Rosenthal implies either (a) that her estimates are inconsistent with the marketing literature and common sense, or (b) that she has failed to demonstrate any effect of marketing on shipments. In either case, her estimated negative value for this parameter indicates that her model cannot provide reliable evidence regarding the influence of detailing on opioid utilization.

D. Professor Rosenthal's Results Do Not Hold When an Appropriate Depreciation Rate Is Used

206. To further test Professor Rosenthal's Model B, I set the depreciation rate at values that are consistent with the academic literature. Other than this adjustment, I fully followed Professor

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[379] For example, Chaloupka (1999) examines cigarette addiction and defines an addictive stock in order to estimate cigarette demand functions. Frank Chaloupka, "Rational Addictive Behavior and Cigarette Smoking," *Journal of Political Economy* 99, no. 4, 1991, pp. 722–742 at p. 726. This stock is a function of past consumption (at p. 732) and uses positive depreciation rates (at Table 1). Similarly, Gruber and Köszegi (2001) analyze the effect of past consumption on current consumption by creating a stock of past consumption, again using positive depreciation rates. Jonathan Gruber and Botond Köszegi, "Is Addiction 'Rational'? Theory and Evidence," *The Quarterly Journal of Economics* 116, no. 4, 2001, pp. 1261–1303 at pp. 1280–1281 and Table V.

[380] Rosenthal Report, ¶ 69.

Rosenthal's methodology to determine the regression coefficients. The results are presented in **Exhibit 15**.

207. The results show that when I use values for the depreciation rate that are consistent with the academic literature, Professor Rosenthal's Model B consistently yields results that contradict those in Table 1 of Professor Rosenthal's expert report. For example, for every depreciation rate in **Exhibit 15** the price index has a positive coefficient, meaning that increases in prices increase sales. This runs counter to basic economic theory and empirical evidence on the effects of opioid prices on opioid consumption, both of which indicate a negative effect of price.[381] Moreover, the signs on the coefficients for the detailing stock during the first sub-period (ending in December 1999) are negative, which under Professor Rosenthal's logic, means that marketing has a negative effect on opioid shipments.

E. Professor Rosenthal's Models Do Not Attempt to Estimate the Impact of Defendants' Allegedly Unlawful Marketing Activities Separately from Defendants' Lawful Marketing

208. The question that needs to be addressed to assist the trier of fact is whether Marketing Defendants' allegedly unlawful marketing activities, as well as the Teva and Actavis Generic Defendants' allegedly unlawful marketing activities, had an impact on shipments of opioids. Professor Rosenthal's direct approach cannot address such a question.

209. As explained in Section IV, Plaintiff alleges that Defendants use different channels to allegedly unlawfully promote opioids. I note that the Complaint lists eight different channels of allegedly unlawful promotions,[382] but Professor Rosenthal only analyzed detailing without providing evidence that detailing is a good proxy for all the other forms of marketing.

210. Additionally, Professor Rosenthal's model does not attempt to estimate the impact of Defendants' allegedly unlawful marketing activities separately from Defendants' lawful marketing activities. This is evident in several ways.

211. First, Professor Rosenthal does not appear to have information on the extent of Defendants' detailing visits that included allegedly unlawful claims versus those that did not.

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[381] Powell et al. (2017) found a price elasticity of demand for opioids of -0.6 for the 59–64 age group using Medicare Part D. See David Powell et al., "How Increasing Medical Access to Opioids Contributes to the Opioid Epidemic: Evidence from Medicare Part D," Working Paper, April 2017, p. 15.

[382] Complaint, ¶ 346.

Professor Rosenthal simply attempts to estimate the impact of Defendants' overall (both allegedly unlawful, and lawful) detailing on aggregate opioid shipments, and in calculating the alleged harm caused by Defendants she assumes that all of Defendants' detailing from 1995 onward was unlawful.[383] She did not review any information regarding the actual marketing engaged in by any Defendant.[384] Thus, she cannot estimate the specific impact of the allegedly false and misleading statements on opioid shipments.

212. Second, Professor Rosenthal asserts that if "a specific Defendant was exempted from liability…, then the measure of harm can be updated to include that Defendants' [sic] promotion in the but-for – and lawful promotion."[385] In other words, she asserts that the coefficients of Model B can be used to predict the effect of lawful and unlawful marketing on opioid shipments for any Defendants.

213. The coefficients in Model B associated with detailing stock represent, according to Professor Rosenthal, an estimate of the effect of one unit of detailing stock on opioids shipments.[386] Therefore, she implicitly assumes that this effect is the same for every manufacturer and is not affected by the nature of the information (lawful or unlawful) that is disseminated. She does not provide any support for these assumptions. In reality, these coefficients reflect the effects of at least three elements: a) the nature of the information used by the sales representatives; b) the quality of the product; and c) the ability of the sales representatives of a specific manufacturer to connect with physicians and to convert the use of this information and product quality into sales. These factors likely imply different manufacturers and different types of marketing should be associated with different coefficients. Indeed, academic literature in other contexts has found that false advertising may reduce sales.[387]

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[383] Rosenthal Report, ¶ 75.
[384] Rosenthal Deposition, 43:19–22. ("I have not, nor do I believe it's necessary to make that causal step, looked at individual details throughout the period for my analysis").
[385] Rosenthal Report, Attachment D.
[386] Rosenthal Report, ¶ 69.
[387] Cawley et al., "The Effect of Deceptive Advertising on Consumption of the Advertised Good and its Substitutes: The Case of Over-the-Counter Weight Loss Products," NBER Working Paper No. 18863, Issued in March 2013; Darke and Ritchie, "The Defensive Consumer: Advertising Deception, Defensive Processing, and Distrust," *Journal of Marketing Research*, Vol. 44, No. 1 (Feb., 2007), pp. 114-127.

214. Third, Professor Rosenthal's Model B assumes a linear effect of detailing stock on MMEs shipped.[388] That is, in any given month, the model assumes that a unit increase in the stock of detailing will always have the same effect on MMEs shipped, regardless of the level of the stock of detailing. In particular, Professor Rosenthal ignores that the academic literature documents decreasing marginal returns for detailing.[389] In other words, academic literature has documented that the marginal effect of the next visit depends on how many detailing visits have already occurred, but Professor Rosenthal's model ignores this fact. This consideration further undermines Professor Rosenthal's Model B ability to predict the effect of Defendants' allegedly unlawful conduct.

215. Therefore, absent any additional evidence, using the same coefficients for the Teva and Actavis Generic Defendants and other manufacturers, or for the Teva and Actavis Defendants' lawful and allegedly unlawful conduct, is unreasonable and leads to flawed and unreliable estimates.

F. Professor Rosenthal's Models Are Unreliable Because of Simultaneity Bias, Reverse Causality, Omitted Variable Bias, and Measurement Error for Price

216. Professor Rosenthal's Model B suffers from multiple additional flaws that undermine the reliability of this model.

1. Simultaneity Bias

217. Econometric principles establish that Professor Rosenthal's method of including price in her model introduces simultaneity bias,[390] which means that even the other coefficients of interest are unreliable and, as a result, the model cannot be used for causal inferences even notwithstanding the other flaws already discussed. In this case, her method of including price would bias the estimated relationship between opioid shipments and detailing stock.

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[388] Rosenthal Report, ¶ 63.
[389] Datta and Dave (2017), p. 457 ("In addition, we also include quadratic terms for all promotional measures to capture diminishing returns.").
[390] William H. Greene, *Econometric Analysis*, Fifth Edition (Upper Saddle River, NJ: Prentice Hall, 2002), p. 379.

2. Reverse Causality

218. There is evidence that opioid shipments affect opioid promotions. As discussed in the Chintagunta report, the Teva Defendants' marketing plans indicate that the Teva Defendants' sales representatives targeted physicians who prescribed higher volumes of Actiq and Fentora.[391] In this case, a positive correlation between shipments and detailing could be the result of shipments causing detailing rather than the result of detailing causing shipments.

3. Omitted Variables Bias

219. An omitted variable occurs when a missing variable influences the dependent variable and is correlated with some explanatory variables. When this happens, the coefficients associated with the explanatory variables reflect the influence of the missing variables, and are therefore biased.[392] As explained earlier in this report, there are several factors that affect opioid shipments that Professor Rosenthal has failed to include in her model.

220. For example, Datta and Dave (2017) emphasize that failing to consider physician characteristics and patient characteristics when analyzing the effect of detailing on physician prescriptions may lead to unreliable results.

> A key empirical concern in this literature relates to potential targeting bias, which physicians who already have a history of prescribing a particular drug or who have a higher unobserved likelihood of prescribing the drug (for instance due to their patient population or practice type) are more likely to be targeted by detailers. Addressing such endogeneity is a vital issue in identifying plausibly causal effects of advertising, which would otherwise lead to overestimates of the advertising response.[393]

221. Another example, as discussed above in Section VII, is that Professor Rosenthal fails to control for product life cycle as is common in the literature seeking to identify the causal effect of promotion on pharmaceutical sales. In general, prescription drug sales are known to expand

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[391] Chintagunta Report, ¶ VII.B.
[392] James H. Stock and Mark W. Watson, *Introduction to Econometrics*, Third Edition (Boston, MA: Addison-Wesley, 2011), p. 180.
[393] Datta and Dave (2017), p. 452.

rapidly after their introduction to the market, and detailing is increasing *also* because of the introduction of new drugs. As Dave and Saffer (2012) explain, "changes in sales, price and promotion are partly governed by the drug's life cycle."[394] In this case, omitting any controls for products' life cycle will cause the regression to misattribute the rise in sales to the marketing, rather than the effects of the introduction of new drugs and products' life cycles.

4. Measurement Error

222. Professor Rosenthal also did not adjust her model for the measurement error related to her price index. She collects her price information from IQVIA to construct her price index.[395] However, as explained by Aitken et al. (2016), "IMS Health's National Sales Perspectives (NSP)…is based on invoiced sales by wholesalers (and direct sales by manufacturers) to their customers, such as major national pharmacy chains, hospitals, clinics, group purchasing organizations, and other supply chain intermediaries. Although the invoiced data incorporate discounts for prompt payment, they typically do not capture off-invoice discounts and rebates frequently given by manufacturers to insurers, providers, and pharmacy benefit managers."[396] Therefore, the use of NSP data by Professor Rosenthal[397] means that her price index is measured with error. Furthermore, even ignoring this issue, Professor Rosenthal does not explain why the prices in NSP are the relevant ones to analyze the effect of prices on opioid shipments, which are the result of a process involving many actors, including patients and insurers.

223. In sum, Professor Rosenthal's models suffer from multiple biases for which she does not account even though the econometric literature provides tools to circumvent these issues. For example, instrumental variables can be used to address the omitted variable bias.[398]

224. Consequently, Professor Rosenthal's model cannot reliably estimate the causal effect of Defendants' allegedly false marketing statements on opioid shipments.

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[394] Dave and Saffer (2012), p. 107.
[395] Rosenthal Report, ¶ 51.
[396] Murray Aitken et al., "Has the Era of Slow Growth for Prescription Drug Spending Ended?" *Health Affairs* 35(9), 2016, pp. 1595–1603.
[397] Professor Rosenthal uses the following NSP files to generate her price index: Highly Confidential NSP_reissue_NDC_1992-2012.xlsx; Copy of NSP 1995 - 2008 reissue 1997.xlsx; Highly Confidential NSP_NDC_Jan 2013-May 2018.xlsx.
[398] Jeffrey M. Wooldridge, *Introductory Econometrics: A Modern Approach*, Fifth Edition (Mason, OH: South-Western, 2013), pp. 512, 532.

G. Professor Rosenthal's Conclusions Regarding the Consequences of Defendants' Alleged Actions Rely on Implausible Assumptions about the Extent of the Allegedly False Marketing and the But-For World

225. In calculating the purported consequences of Defendants' allegedly false marketing activities in Table 2 and 3, Professor Rosenthal assumes that all of Defendants' detailing activities are false, and moreover, that none of these detailing expenditures would occur in the but-for world. Both of these assumptions are implausible.

226. First, there is no evidence about the extent to which Defendants' marketing activities were false. As discussed in the Chintagunta report, Teva had non-false marketing activities.[399] Thus, even apart from the various flaws in Professor Rosenthal's models, her estimates in Table 2 and 3 would overestimate the impact of the allegedly false marketing on opioid shipments.

227. Second, Professor Rosenthal does not explain why detailing visits would decrease absent the allegedly false statements. That is, it is possible that absent the allegedly false marketing statements the detailing visits would remain the same or could even increase, with merely a change in messaging. Even if they were to decrease, it is unclear by how much, and Professor Rosenthal has no basis to assume that they would go down to zero.

228. Third, as explained in Section XI., Professor Rosenthal does not establish that the Model B coefficients can be used to estimate the but-for world because these coefficients may vary by 1) manufacturer, 2) type of marketing (lawful or unlawful), and 3) levels of detailing (diminishing marginal return). These considerations are critical for the but-for world since the goal is to predict the number of MMEs that would have been shipped had a specific Defendant only used lawful marketing.

229. Therefore, Professor Rosenthal's calculations to estimate but-for MMEs for Defendants are baseless.

[399] Chintagunta Report, ¶ VI.B.

XII. Professor Rosenthal's Indirect Approach Suffers from Multiple Flaws and Is Unreliable

230. In addition to the direct approach, Professor Rosenthal proposes a second econometric approach, which she calls the "indirect approach." She motivates this approach by claiming that the direct approach could not "include…all of the tactics allegedly employed by the Defendants, including manipulation of various professional societies and accrediting bodies."[400]

231. After briefly describing this indirect approach, I explain why this methodology is unreliable and speculative. Subsequently, as I did with the direct approach, I demonstrate that when depreciation rates that are consistent with the academic literature are used to estimate the detailing stock, Professor Rosenthal's assertion that her measure of excess MMEs using the indirect approach is related to the alleged misconduct is unsupported. Thus, her methodology is unreliable.

A. Overview of Professor Rosenthal's Indirect Approach

232. Professor Rosenthal's indirect methodology starts with a regression analysis conducted at the county level in 1997. Her goal is to analyze the influence of demographic, economic, and healthcare characteristics of an area on opioid shipments prior to the misconduct. Professor Rosenthal asserts that using 1997 as the benchmark makes her analysis likely to be conservative.[401] As explained in the next section, she provides no evidence to support this assertion.

233. To perform this regression analysis, she collects opioid shipments for the county sample used in the mortality analysis (404 counties)[402] and calculates opioid shipments per capita, per day. Then, for each county in 1997, she chooses a set of explanatory variables that include demographic information (e.g., percent of the population in different age groups), economic information (e.g., unemployment rate, employment-to-population ratio), and information about two healthcare factors—the percentage of the population without insurance coverage and the number of cancer deaths.[403] Then, she regresses opioid shipments on these explanatory variables

[400] Rosenthal Report, ¶ 78.
[401] Rosenthal Report, ¶ 79.
[402] Rosenthal Report, Table 4.
[403] Rosenthal Report, ¶ 84.

at the county level to obtain the estimates she presents in Table 4. Next, to estimate the portion of MMEs for the years 1998–2016 that was due to demographic, economic, and healthcare characteristics of these 404 counties, Professor Rosenthal assumes 1) that her chosen variables capture all of the relevant demographic, economic, and healthcare factors and 2) that the coefficients from this first regression can be applied to future years—that is, that there should be a stable relationship between these factors and opioid shipments over time. Specifically, she collects the same explanatory variables for each of these years and applies the 1997 coefficients to predict MME shipments for each year in a manner that she claims accounts for changes in these explanatory variables.[404]

234. Then, Professor Rosenthal adds to these predicted MME shipments "an annual increase based on an estimated linear trend using historical data [about opioid shipments] that pre-date the alleged misconduct."[405] In particular, she estimates this trend using the period 1980–1995.[406] She asserts that this linear trend captures "the market expanding effect of non-Defendant promotion"[407] and the "changes in clinical practices and other unmeasured influences."[408]

235. Professor Rosenthal includes one final adjustment to estimate MME shipments that would have occurred but for the alleged marketing misconduct: She adjusts for the effect of increasing prices on opioids shipments.[409] She starts with the price index coefficient from the direct approach that was determined based on monthly, national data. Then, she makes an adjustment for the difference in magnitude between opioid shipments in the data that she uses for the indirect approach and opioid shipments in the data she uses for the direct approach. Finally, she multiplies this adjusted coefficient by the increase in the price index for each year to yield the effect of prices on predicted MMEs. She then estimates the level of opioid shipments that would have occurred absent the Defendants' alleged misconduct—the "but-for MMEs"—by summing the predictions from the regression on demographic, economic, and health characteristics; the adjustment for the linear trend; and the adjustment for rising prices.

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[404] Rosenthal Report, ¶ 87.
[405] Rosenthal Report, ¶ 87.
[406] Rosenthal Report, ¶ 87.
[407] Rosenthal Report, ¶ 81.
[408] Rosenthal Report, ¶ 87.
[409] Rosenthal Report, ¶ 88.

236. After estimating the but-for MMEs for each year, Professor Rosenthal allocates the full difference between the actual MMEs and but-for MMEs ("excess MMEs") to "the full set of tactics used by the Defendants to increase opioids use."[410] She denotes this as a "residual analysis" and appeals to prior literature that uses this approach "to evaluate economic impact."[411]

B. Professor Rosenthal's Indirect Approach is Conceptually Flawed

237. As explained in the previous section, Professor Rosenthal's indirect approach uses a "residual analysis" to estimate the impact of the allegedly false marketing activities on opioid MMEs. She interprets the difference between predicted and actual MMEs as due to the allegedly unlawful marketing activities. Predicted MMEs are estimated based on a regression of opioid MMEs on a set of economic, demographic, and health care characteristics of counties in 1997, as well as a linear time trend and a price index.[412]

238. Professor Rosenthal finds that her model, after adjusting for the linear time trend and the price index, leads to predicted MMEs that are lower than actual MMEs, and she interprets this residual as being caused by Defendants' allegedly unlawful marketing activities. However, Professor Rosenthal's choice to interpret this under-prediction as caused by marketing is unsupported by the literature in health economics. This academic literature, including three articles she cites, typically interprets the residuals as due to technological change.[413] In addition,

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[410] Rosenthal Report, ¶ 82.
[411] Rosenthal Report, ¶ 82.
[412] Rosenthal report, ¶¶ 78–82.
[413] Sheila Smith et al., "Income, Insurance, and Technology: Why Does Health Spending Outpace Economic Growth?" *Health Affairs* 28, no.5, 2009, pp. 1276-1284 at Exhibit 1; Paul B. Ginsburg, "High and Rising Health Care Costs: Demystifying U.S. Health Care Spending," Robert Wood Johnson Foundation Research Synthesis Report 18, 2008 at Table 1; Joseph P. Newhouse, "Medical Care Costs: How Much Welfare Loss?" *The Journal of Economic Perspectives* 6, no. 3, 1992, pp. 3–21 at p. 5. CBO, "Technological Change and the Growth of Health Care Spending", January 2018, available at http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/89xx/doc8947/01-31-techhealth.pdf, p. 7. ("Another way to approximate the effect of technological change is to do so indirectly, using the "residual" method. Certain demographic and economic factors, such as the aging of the population and rising personal income, are determinants of health care spending; using estimates of the relationships between those factors and spending levels, analysts can estimate how changes in those factors contributed to changes in spending, assuming no changes in medical technology. After accounting for the contributions of as many measurable factors as possible, analysts attribute the unexplained portion of spending growth, or the residual, to technological change and the changes in clinical practice associated with it. This approach yields findings that can be sensitive to assumptions concerning the effects of the various factors. In addition, studies using this approach generally do not account for dynamic interactions between growth of personal income, health insurance coverage, and technology development. Nonetheless, this approach can

other factors are omitted from Professor Rosenthal's model that also contribute to its systematic under-prediction of opioid shipments. These factors include, for example, the expansion of insurance coverage for pharmaceuticals generally and opioids specifically,[414] and the interaction between technology and health insurance.[415] Using the "residual approach" to interpret the under-prediction as caused by a single omitted factor requires that all other factors be fully accounted for. However, key factors that are omitted likely contributed to growth in opioid use during this time period, and Professor Rosenthal fails to demonstrate that her linear trend accounts for them properly.

239. Thus, as I will further explain below, what Professor Rosenthal interprets as the effect of marketing in fact does not isolate the effect of marketing, but includes the effect of many other factors.

C. The Different Components of Professor Rosenthal's Indirect Approach Are Not Correctly Estimated

240. As explained in section XII.A, the three components of Professor Rosenthal's indirect approach—1) the 1997 cross-sectional regression,2) the time trend, and 3) the price index that are used to estimate but-for MMEs—are individually unreliable, and so is her conclusion that her excess MMEs are caused solely by Defendants' alleged unlawful tactics.

1. The 1997 Cross-Sectional Regression

241. The first component is the cross-sectional regression analysis performed for 404 counties using socioeconomic and healthcare factors that were collected for 1997 as explanatory variables. Professor Rosenthal uses the estimated coefficients to predict shipments in subsequent years, which assumes that 1) the coefficients of her regression are correct, and 2) these

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yield a reasonable approximation of how technological change relates to long-term growth in total health care spending.")

[414] Zhou et al., "Payments For Opioids Shifted Substantially To Public and Private Insurers While Consumer Spending Declined, 1999-2012." *Health affairs (Project Hope)*, 35, no. 5, 2016, pp. 824–831.

[415] Sheila Smith et al., "Income, Insurance, and Technology: Why Does Health Spending Outpace Economic Growth?" *Health Affairs,* 28, no. 5, 2009, pp. 1276-1284 at Table 1; Burton A Weisbrod, "The Health Care Quadrilemma: An Essay on Technological Change, Insurance, Quality of Care, and Cost Containment." *Journal of Economic Literature*, 29, no. 2, 1991, pp. 523–532.

coefficients do not change over time. However, she does not provide any evidence that these two conditions are met.

242. The first condition is that the coefficients are estimated correctly. This is unlikely to be true; the regression analysis suffers from some of the same flaws as those detailed for the direct approach, and this would bias the coefficients. In particular, Professor Rosenthal's cross-sectional analysis suffers from endogeneity and omitted variable biases. The omitted variable issue is particularly important for the residual analysis because these missing variables will be included in the residual. Professor Rosenthal argues that the effect of these missing variables is included in her secular trend, but I will explain that it is not the case.

243. For example, Datta and Dave (2017) indicate that it is important to control for "disease prevalence…and provider availability."[416] Professor Rosenthal's controls for the prevalence of diseases that could require the use of opioids are insufficient; while it is necessary to control for the prevalence and severity of *all* the illnesses that might be associated with opioid use, Professor Rosenthal only controls for cancer deaths.[417] In Section X of her own expert report, Professor Rosenthal indicates that opioids could be used for other conditions such as the "short-term treatment of severe acute pain (e.g., trauma or post-surgical pain); end-of-life pain/hospice care" and others, thereby admitting that cancer deaths alone are an insufficient control.[418]

244. Also, as explained in Section XI.F. 3., omitted variables can bias coefficients, which would undermine the reliability of Professor Rosenthal's cross-sectional regression.

245. The second condition is that the coefficients she estimates for the 1997 cross-section are applicable to the period from 1998–2016. In other words, she assumes that the relationship between her socioeconomic and healthcare variables and opioid shipments is constant over time. She provides no empirical evidence or academic support for such an assumption.

246. The age-aggregation bias is a good illustration of this issue. If these counties age over time then the average age within the age buckets chosen by Professor Rosenthal may increase over time. If age is related to opioid shipments even conditional on age bucket, then the coefficients associated with Professor Rosenthal's age buckets are going to change over time.

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[416] Datta and Dave (2017), p. 457.
[417] Rosenthal Report, Table 4.
[418] Rosenthal Report, ¶ 92.

247. Professor Rosenthal also conducted her cross-sectional regression on data that she admits is inappropriate. As she explains, this regression analysis should have been conducted during a period prior to the alleged misconduct,[419] but she performs this analysis using information collected in 1997, a year that was allegedly tainted according to her.[420] She tries to downplay this problem by claiming that Defendants' alleged misconduct in 1997, which allegedly elevated shipments, will lead to conservative estimates of harm. However, such a statement implicitly admits that not including any variables about the alleged misconduct in her regression analysis could bias her results. She offers no evidence that omitting these variables will, as claimed, bias upwards the estimates of but-for shipments. The overall effect depends on the existence and sign of the correlation between the omitted variables and the variables already included as explanatory variables.

248. Moreover, Professor Rosenthal's claim that her estimate of but-for MMEs is conservative is undermined by her own work. She fails to mention in the body of her report that she performs a downward adjustment to her estimates of but-for MMEs. Specifically, she uses the linear trend that she develops based on shipment data for the period 1980–1995 (discussed in more detail in the next subsection), and she calculates the difference between the actual increase in opioid shipment for the period 1995–1997 and the prediction of this trend line. Then, she removes this difference, which she calls "excess shipment," from her estimates of but-for MMEs in 1997 and for every year going forward.[421] In attachment D, Professor Rosenthal indicates that "IQVIA data is used to estimate the conversion to an earlier benchmark year, by incorporating an adjustment to these results to reflect changes in shipments between 1995 and 1997."[422] However, she does not explain the logic behind this adjustment and, in particular, that it is a downward adjustment.

249. These flaws show that the cross-sectional regression used by Professor Rosenthal is unreliable.

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[419] Rosenthal Report, ¶ 79.
[420] Rosenthal Report, Attachment D.
[421] Rosenthal Report Attachment D.
[422] Rosenthal Report, Attachment D.

2. The Secular Trend

250. The second component of the indirect approach's estimate of but-for MMEs is also unreliable. Professor Rosenthal adds to her estimates of but-for MMEs a secular trend to capture "the market expanding effect of non-Defendant promotion"[423] and the "changes in clinical practice and other unmeasured influences."[424] To do so, she estimates a linear trend relying on shipment data from the International Narcotics Control Board for the period 1980–1995. The assertion that such a calculation yields an appropriate adjustment is unsupported.

251. Professor Rosenthal's linear trend line assumes that the overall effect on opioid shipments of non-Defendants' marketing and other variables that she omitted—such as the competition from other drugs, the effects of product life cycle, the introduction of new products, the establishment of new clinical knowledge, among other items—yields a constant increase for every year in the period 1998–2016. Professor Rosenthal does not provide any academic support for this assumption, and it is unreasonable. In fact, the variables that are supposed to drive this linear trend are dynamic in nature; their annual changes are not constant over time. Therefore, it is unreasonable to assume that the change in their effects on opioid shipments from one year to the next is constant over time.

3. The Price Index

252. The last component of Professor Rosenthal's indirect approach to estimate but-for MMEs is the adjustment for rising prices. As discussed above, she uses the coefficient on the price index that was estimated by the direct approach. Also as explained above, during the discussion of the direct approach, the influence of prices on shipments is complex because these variables are simultaneously determined by market outcomes. Because the methodology of the direct approach was incorrect, using the coefficient from the direct approach for the indirect approach also results in an unreliable methodology.

253. In summary, Professor Rosenthal's conclusion that the differences between actual MMEs and her estimates of but-for MMEs represent the number of MMEs caused by the alleged

[423] Rosenthal Report, ¶ 81.
[424] Rosenthal Report, ¶ 87.

misconduct is baseless. The previous considerations clearly show that her methodology is flawed and, therefore, these "excess MMEs" represent the influence of multiple variables on MMEs—not only the influence of the alleged misconduct.

D. There Is No Evidence that Professor Rosenthal's Excess MMEs Are Related to The Alleged Misconduct

254. Professor Rosenthal asserts that 1) "[t]he manufacturer Defendants used a panoply of both branded and unbranded marketing tactics," 2) "pharmaceutical marketing programs typically combine various forms of marketing such that, were there to be an increase or decrease in promotional detailing, it is reasonable to expect that some other forms followed [sic] that course," and 3) "detailing is a good proxy for total promotional effort."[425]

255. She provides no evidence for these assertions. Assuming Professor Rosenthal's assertions are correct and her estimates of excess MMEs were related to the alleged misconduct, then a strong, positive correlation should exist between these excess MMEs for the 404 counties and detailing stocks.

256. To evaluate the validity of her assertion and estimates, I test this implication. Specifically, I calculate the correlation between the yearly excess MMEs estimated by Professor Rosenthal's indirect method and the average monthly detailing stock for each year. Even though the measure of detailing stock is national, one would expect that the detailing stock for these 404 counties is strongly positively correlated with the nationwide detailing stock. To calculate the detailing stock, I use Professor Rosenthal's calculations making only one adjustment: instead of her negative depreciation rate, I consider the same set of literature-supported depreciation rates as I considered in my discussion of the direct approach above.

257. **Exhibit 16** shows that the Pearson correlations are small for this set of depreciation rates. The correlation coefficients are from 0.28% to 12.01%, failing to support Professor Rosenthal's conclusion that her estimated excess MMEs are the result of marketing.

[425] Rosenthal Report, ¶ 56.

XIII. Professor Rosenthal's Analysis to Test the "Under-Treated Pain" Theory Is Unreliable

258. Professor Rosenthal purports to examine whether the rise in opioid prescribing could be explained by the fact that the pain was previously "under-treated." To do so, she conducts a "thought experiment" in order to calculate an "'upper bound' of how much of the growth in MMEs could be attributable to more intensive pain management for patient groups that, according to plaintiffs' experts could have benefitted from treatment with opioids."[426]

259. The first step of her "thought experiment" is to select, based on the inputs of other Plaintiffs' experts, pain conditions for which the use of opioids is properly indicated.

> "As a general matter and for purposes of this empirical test, I assume: (i) that, at most, opioids are properly indicated for the short-term treatment of severe acute pain (e.g. trauma or post-surgical pain); end-of-life pain/hospice care; and cancer pain from active malignant disease; (ii) that chronic opioid therapy is not recommended for most common chronic pain conditions (defined as moderate to severe pain lasting beyond 60 to 90 days), including low back pain, centralized pain such as fibromyalgia, and headache pain; and (iii) that in less common chronic pain conditions (such as pain from advanced multiple sclerosis, sickle cell disease, pain following spinal cord injury and paraplegia, or post-herpetic neuralgia), which comprise a small percentage of chronic pain patients, opioids may be considered a third-line therapy (taken if other therapies are ineffective or contraindicated) for moderate and severe pain."[427]

260. She also adds that "[g]iven the narrow categories of indicated chronic pain use, its role as third-line therapy, and the significant risks associated with its use, optimal chronic opioid therapy is difficult to characterize"[428] For these reasons, she did not attempt to "capture optimal treatment for patients with chronic pain in [her] simulation."[429] In other words, Professor Rosenthal did not include any use of opioids related to chronic pain in her analysis.

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[426] Rosenthal Report, ¶ 92.
[427] Rosenthal Report, ¶ 92.
[428] Rosenthal Report, ¶ 93.
[429] Rosenthal Report, ¶ 93.

261. Then, for each of these conditions Professor Rosenthal estimates 1) the number of patients treated, 2) a baseline assumption regarding the daily dose in MMEs, and 3) an estimated duration of treatment in days.[430] Finally, she multiplies these three estimates for each type of pain condition and sum these products in order to obtain the "theoretical maximum" use of opioids.[431] She also performs a sensitivity test by increasing her results by 50%.[432]

262. However, Dr. Michna and Dr. Rosenblatt both state that opioids can be appropriate and effective for treating chronic non-cancer pain under certain circumstances.[433] In particular, whereas Professor Rosenthal specifically excludes chronic pain due to fibromyalgia from her analysis,[434] Dr. Michna states that opioids can be effective in treating fibromyalgia, in addition to other causes of chronic pain such as sickle cell disease and nociceptive or neuropathic pain.[435,436]

263. Professor Rosenthal also does not consider other factors that may cause opioid MMEs to increase. Based on these reasons, Professor Rosenthal's analysis of under-treated pain is unreliable.

XIV. Conclusion

264. In conclusion my review of documents related to this matter leads me to conclude that the risks of opioids in general, and of the Teva and Actavis Generic Defendants' opioids in particular, were generally known, or should have been known, to informed actors, including the Plaintiffs, in the U.S. during the period of the allegations. Given this information and the tools available to them, these actors could have taken measures to limit opioid use in Ohio. This is not considered by Plaintiffs and Plaintiffs' experts, who also do not evaluate TPPs' financial incentives to encourage opioid use.

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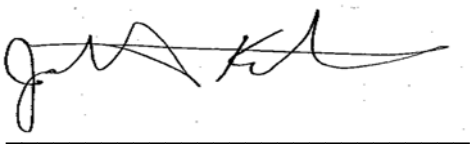
[430] Rosenthal Report, ¶ 94.
[431] Rosenthal Report, ¶ 94.
[432] Rosenthal Report, ¶ 101.
[433] Expert Report of Professor Edward Michna, J.D., M.D, May 10, 2019, ("Michna Report"), ¶ 37-41; Expert Report of Melanie H. Rosenblatt, M.D., May 10, 2019, ("Rosenblatt Report"), ¶ 37, 39-43.
[434] Rosenthal Report, ¶ 92.
[435] Michna Report, ¶ 40.
[436] I note that the Centers for Disease Control and Prevention also recommends the use of opioids for chronic pain when appropriate. *See* Dowell et al. "CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016," Morbidity and Mortality Weekly Report, 65(No. RR-1), 2016.

265. Professor Gruber has failed to establish a causal relationship between opioid shipments and opioid abuse and mortality. His conclusions fail to account for a host of other factors, often acknowledged by Professor Gruber himself that can influence opioid abuse. He also makes unsubstantiated claims regarding the link between prescription opioid shipments and the use of illicit opioids, and fails to consider important differences between medical and nonmedical use of prescription opioids, and how these difference are related to future illicit opioid use.

266. Likewise, Professor Rosenthal's direct and indirect approaches suffer from multiple flaws, are unreliable, and cannot reliably establish a causal relationship between Defendants' alleged promotion of opioids and opioid shipments. They certainly cannot reliably establish a causal relationship between the Teva and Actavis Defendants' alleged promotion of opioids and opioid shipments.



Jonathan Ketcham, PhD, 5/10/2019

EXHIBIT 1

Curriculum Vitae
May 2019

JONATHAN D. KETCHAM, PH.D.

Department of Marketing
W. P. Carey School of Business
Arizona State University
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CURRENT POSITIONS

2016-	Earl G. and Gladys C. Davis Distinguished Research Professor in Business, Department of Marketing, W.P. Carey School of Business, Arizona State University
2017-	Faculty Affiliate, Department of Economics, W.P. Carey School of Business, Arizona State University

PREVIOUS ACADEMIC POSITIONS

2010-2016	Associate Professor with tenure, Department of Marketing, W.P. Carey School of Business, Arizona State University
2005-10	Assistant Professor, School of Health Management and Policy, W.P. Carey School of Business, Arizona State University
2002-04	Visiting Scholar, Robert Wood Johnson Foundation Scholars in Health Policy Research Program, University of California, Berkeley and UCSF

EDUCATION

Ph.D. Economics, The Wharton School of Business, University of Pennsylvania. 2002.

B.A. Economics, *magna cum laude*. Baylor University. 1997.

PEER-REVIEWED PUBLICATIONS

1. Michael Keane, Jonathan Ketcham, Nicolai Kuminoff, and Timothy Neal. *Forthcoming*. "Evaluating Consumers' Choices of Medicare Part D Plans: A Study in Behavioral Welfare Economics." **Journal of Econometrics**. Also NBER working paper #25652.

2. Jonathan Ketcham, Nicolai Kuminoff, and Christopher Powers. 2019. "Estimating the Heterogeneous Welfare Effects of Choice Architecture: An Application to the Medicare Prescription Drug Insurance Market." **International Economic Review**. Also NBER working paper #22732.

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3. Jonathan Ketcham, Nicolai Kuminoff, and Christopher Powers. 2016. "Choice Inconsistencies among the Elderly: Evidence from Plan Choice in the Medicare Part D Program: Comment." **American Economic Review**, 106(12): 3932-61. Also NBER working paper #21387.

4. Jonathan Ketcham, Claudio Lucarelli, and Christopher Powers. 2015. "Paying Attention or Paying Too Much in Medicare Part D." **American Economic Review**, 105(1): 204-233.

5. Andrew Epstein and Jonathan Ketcham. 2014. "Information Technology and Agency in Physicians' Prescribing Decisions." **RAND Journal of Economics**, 45(2): 422-448.

6. James Niels Rosenquist, Jonathan Ketcham, Haizhen Lin and Kosali Simon. 2013. "The Impact of the 2006-2009 United States Housing Crisis on Antidepressant Medication Utilization." **Economics Letters**, 121: 449-453.

7. Jonathan Ketcham, Claudio Lucarelli, Eugenio Miravete and M. Christopher Roebuck. 2012. "Sinking, Swimming, or Learning to Swim in Medicare Part D." **American Economic Review**, 102(6): 2639-2673.

8. Andrew Epstein, Jonathan Ketcham, Saif Rathore and Peter Groeneveld. 2012. "Variations in Access to Innovation by Payer: The Case of Drug-Eluting Stents." **Medical Care**, 50(1): 1-9.

9. Andrew Epstein, Jonathan Ketcham, and Sean Nicholson. 2010. "Specialization and Matching in Professional Firms." **RAND Journal of Economics**, 41(4): 812–835. Also NBER working paper #14070.

10. Saif Rathore, Jonathan Ketcham, G. Caleb Alexander, and Andrew Epstein. 2009. "Influence of Patient Race on Physician Prescribing Decisions: A Randomized On-line Experiment." **Journal of General Internal Medicine**, 24(11): 1183-91.

11. Jonathan Ketcham, Karen Lutfey, Eric Gerstenberger, Carol Link and John McKinlay. 2009. "Physician Clinical Information Technology and Health Care Disparities." **Medical Care Research and Review**, 66(6): 658-681.

12. Jonathan Ketcham and Kosali Simon. 2008. "Medicare Part D's Effects on Elderly Drug Costs and Utilization." **American Journal of Managed Care**, 14(11): SP14-22. Also NBER working paper #14326.

13. Jonathan Ketcham and Jeffrey Ngai. 2008. "How Similar are States' Medicaid Preferred Drug Lists?" **American Journal of Managed Care**, 14(11): SP46-52.

14. Andrew Epstein, Saif Rathore, G. Caleb Alexander, and Jonathan Ketcham. 2008. "Primary Care Physicians' Views on Medicare Part D." **American Journal of Managed Care**, 14(11): SP5-13.

15. Jonathan Ketcham and Michael Furukawa. 2008. "Hospital-Physician Gainsharing in Cardiology." **Health Affairs** 27(3): 803-812.

16. Glenn Melnick and Jonathan Ketcham. 2008. "Have HMOs Broadened their Hospital Networks: Changes in HMO Hospital Networks in California, 1999-2003." **Medical Care** 46(3): 339-342.

17. Jonathan Ketcham and Andrew Epstein. 2008. "Medicaid Preferred Drug Lists' Costs to

Physicians." **Medical Care** 46(1): 9-16.

18. Michael Furukawa, Jonathan Ketcham and Mary Rimsza. 2007. "Physician Practice Revenues and Use of Information Technology in Patient Care." **Medical Care**. 45(2): 168-176.

19. Jonathan Ketcham, Laurence Baker, and Donna MacIsaac. 2007. "Physician Practice Size and Variations in Treatments and Outcomes: Evidence from Medicare Patients with Acute Myocardial Infarction." **Health Affairs**. 26(1): 195-205.

20. Jonathan Ketcham and Andrew Epstein. 2006. "Which Physicians are Affected Most by Medicaid Preferred Drug Lists for Statins and Antihypertensives?" **PharmacoEconomics**. 24(S3): 27-40.

21. Karen Lutfey and Jonathan Ketcham. 2005. "Patient and Provider Assessments of Adherence and the Source of Disparities: Evidence from Diabetes Care." **Health Services Research**. 40(6): 1803-1817.

22. Kevin Volpp, Jonathan Ketcham, Andrew Epstein, and Sankey Williams. 2005. "The Effects of Price Competition and Reduced Subsidies for Uncompensated Care on Hospital Mortality." **Health Services Research**. 40(4): 1056-1077.

23. Daniel Eisenberg and Jonathan Ketcham. 2004. "Economic Voting in US Presidential Elections: Who Blames Whom for What." **The Berkeley Electronic Journal of Economic Analysis & Policy**. 4(1): Article 19.

24. Patricia Danzon and Jonathan Ketcham. 2004. "Reference Pricing of Pharmaceuticals for Medicare: Evidence from Germany, the Netherlands, and New Zealand." **Forum for Health Economics and Policy** (The Berkeley Electronic Press). 7(1): Article 2. Also NBER working paper #10007.

WORKING PAPERS

Kelly Bishop, Jonathan Ketcham, and Nicolai Kuminoff. "Hazed and Confused: The Effect of Air Pollution on Dementia." *NBER working paper #24970.*

Jonathan Ketcham, Pierre Léger and Claudio Lucarelli. "Group Incentives and Standardization: An Application to Hospital-Physician Gainsharing." *Revise and resubmit*, **RAND Journal of Economics**.

Jonathan Ketcham, Sean Nicholson, and Lawrence Casalino. "Relative Prices, Payer Mix and Regional Variations in Medical Care."

Gautam Gowrisankaran, Jonathan Ketcham, Yujia Peng, Arundhati Tillu. "Do Physicians Learn about Technology from Experience or the Literature? Evidence from Coronary Stents."

Jonathan Ketcham, Nicolai Kuminoff and Nirman Saha. "The Values of a Statistical Life among the Medicare Population."

Jonathan Ketcham, Nicolai Kuminoff, and Christopher Powers. "Rejoinder to Abaluck and Gruber." December 2016. https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2884875

GRANTS AND SPONSORED PROJECTS

Principal Investigator, Banner Health. "Predicting Future Spending." 2015-2016. $70k.

Principal Investigator, NIHCM Foundation. "Identifying Winners and Losers Under Proposals to Simplify Drug Plan Choice in Medicare Part D," with Nicolai Kuminoff, Co-Principal Investigator. 2014, $50k.

Principal Investigator, R01, Agency for Healthcare Research and Quality. "Relative Price, Payer Mix and Regional Variations," with Sean Nicholson and Lawrence Casalino, Co-Investigators. 2013-2015, R01 HS022306-01. $454k.

Principal Investigator, R01, Agency for Healthcare Research and Quality. "Hospital-Physician Gainsharing," with Claudio Lucarelli, Co-Investigator and Pierre Léger, Consultant. 2009-2011, R01 HS018481-01. $484k.

Consultant, Upstate Health Research Network for FAIR Health. 2010-2012.

Consultant, California HealthCare Foundation. "Economic Performance in Orthopedics and Cardiology," with James Robinson through University of California, Berkeley. 2009-2010.

Co-Principal Investigator, Pfizer Inc. "The Effect of Medicare Part D on Access to Prescription Drugs" with Kosali Simon through Cornell University. 2007. $60k.

Principal Investigator, R13 HS016883-01, Agency for Healthcare Research and Quality. "The 18th Annual Health Economics Conference." 2007-2008. $50k.

Principal Investigator, Health Sector Supply Chain Research Consortium, W.P. Carey School of Business, Arizona State University. "Physician-Hospital Collaboration for Supply Chain Management: Implications of Value Analysis Teams and Gainsharing" with Michael Furukawa and Gene Schneller. 2005-2006. $100k.

Principal Investigator, Agency for Healthcare Research and Quality dissertation grant award. "Medical group responses to HMO selective contracting." 2002.

AWARDS AND HONORS

Stanford Institute for Economic Policy Research visiting professor, 2019-2020.

NIHCM Foundation's Annual Health Care Research Award finalist, 2016.

Hoover Institution visiting fellow, 2015-2016.

NIHCM Foundation's Annual Health Care Research Award winner, 2013.

Faculty Achievement Award, Defining Edge Research and Creative Work, Best Professional Application (ASU university-wide award), 2013.

John D. Thompson Prize for Young Investigators. Awarded by the Association of University Programs in Health Administration, 2010.

Most Outstanding Abstract, AcademyHealth Annual Research Meeting. "Within Hospital Payer and Race Differences in the Early Use of Drug-Eluting Coronary Stents" with Andrew Epstein et al. 2006.

National Research Service Award doctoral fellow, Agency for Health Care Policy and Research. Health Care Systems Department, Wharton, University of Pennsylvania. 1997-2000.

Phi Beta Kappa, Baylor University. 1997.

National Merit Scholarship, Baylor University. 1993–1997.

INVITED PRESENTATIONS 2015-2019

2019
American Society of Health Economists Conference.

2018
American Society of Health Economists Conference.

Tulane University, Department of Economics.

Society for Consumer Psychology Conference.

2017
Annual Health Economics Conference, University of Southern California.

Emory University, Department of Economics.

2016
Annual Health Econometrics Workshop.

University of Arizona, Eller College of Management, Marketing.

American Society of Health Economists Conference.

University of California San Diego, Rady School of Business, Marketing.

Stanford University and Hoover Institution.

University of Chicago, Booth School of Business, Marketing.

University of Illinois, Center for Business and Public Policy.

Vanderbilt University, Owen School of Management.

American Economic Association Annual Meeting, San Francisco, CA.

2015

University of Southern California, Sol Price School of Public Policy.

Quantitative Marketing and Economics Conference, Massachusetts Institute of Technology, Sloan School of Management.

Annual Health Economics Conference, University of Georgia.

Yale University, Institution for Social Policy Studies.

International Health Economics Association Congress, Milan, Italy.

Kellogg School of Management's 4th Annual Conference on Healthcare Markets, Northwestern University.

Cornell University, Policy Analysis and Management.

Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation.

Congressional Budget Office.

TEACHING

Courses taught

"Health Care Economics." MBA programs, W.P. Carey School of Business. 2007-present.

"Marketing Research." Undergraduate marketing course, W.P. Carey School of Business. 2013-present.

"Economics of Health Care." Mayo Clinic Physician Leadership Business Academy, Executive Education, W.P. Carey School of Business. 2015-2016.

"Health Economics, Policy, and Payment Methods." Master of Science in the Science of Health Care Delivery, ASU. 2013.

"Health Care Economics." Undergraduate economics course, W.P. Carey School of Business. 2010-2011.

"Internship Seminar." MHSM program, W.P. Carey School of Business. 2010.

"Health Sector Information Management." MBA and MHSM programs, W.P. Carey School of Business. 2005-2007.

"Health Care Organizations." Undergraduate program, W.P. Carey School of Business. 2005-2006.

"Introduction to the US Healthcare System." Health Care Systems Department, The Wharton School, University of Pennsylvania. 2000-2001.

Dissertation Committees

Member, Sophie Mathes (current)
Member, Nirman Saha (current)
Member, Tomas Sanguinetti (current)
Member, Ranjit Christopher Magendraraj (2015)

EXTERNAL PROFESSIONAL SERVICE

Program Chair, "Consumer Decision Making in Health Care," 2019 American Society of Health Economists Conference.

Program Chair, "Consumer Decision Making in Health Care," 2018 American Society of Health Economists Conference.

Selection Committee member, John D. Thompson Prize for Young Investigators, AUPHA. 2013-current.

Advisory Board Member, Center for Health and Economy, 2012-current.

Steering committee member, Annual Health Economics Conference, 2009-current.

Scientific review committee member for the Agency for Healthcare Quality and Research, 2015-2018.

Awards committee member, American Society of Health Economists, 2012-2015.

Scientific review committee member for the National Institutes of Health, 2012, 2015, 2016.

Upstate Health Research Network consultant to FAIR Health. 2010-2012.

Coordinator, 18th Annual Health Economics Conference, 2007.

Book reviewer for Cambridge University Press, 2009.

Referee on articles for numerous peer-reviewed journals

PROFESSIONAL MEMBERSHIPS

American Economic Association
American Society of Health Economists
The Econometric Society
Heterodox Academy

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EXHIBIT 1

Prior Testimony of Jonathan D. Ketcham

Deposition, *State of Oklahoma, ex rel., Mike Hunter, Attorney General of Oklahoma v. Purdue Pharma L.P., et al.*, No. CJ-2017-816, District Court of Cleveland County, Oklahoma, March 2019.

EXHIBIT 2

List of Documents Considered

Document Title, Bates Numbers	Document Date
Legal Pleadings	
Corrected Second Amended Complaint and Jury Demand, *The County of Summit, et al. v. Purdue Pharma L.P., et al.*	May 18, 2018
Second Amended Corrected Complaint and Demand for Jury Trial, *City of Cleveland, et al. v. Purdue Pharma L.P., et al.*	May 29, 2018
Second Amended Corrected Complaint and Demand for Jury Trial, *The County of Cuyahoga et al. v. Purdue Pharma L.P. et al*	May 25, 2018
Third Amended Complaint and Jury Demand, *The County of Summit et al. v. Purdue Pharma L.P. et al*	March 21, 2019
Expert Reports	
Expert Report of Melanie H. Rosenblatt, M.D.	May 10, 2019
Expert Report of Pradeep K. Chintagunta, Ph.D.	May 10, 2019
Expert Report of Professor David Cutler	March 25, 2019
Expert Report of Professor Edward Michna, J.D., M.D.	May 10, 2019
Expert Report of Professor Jonathan Gruber and Production Materials	March 25, 2019
Expert Report of Professor Meredith Rosenthal and Production Materials	March 25, 2019
Expert Report of Sean Nicholson, Ph.D.	May 10, 2019
Expert Report of Professor Thomas McGuire (Damages to Bellwethers)	March 25, 2019
Report of Professor Thomas McGuire Regarding Public Nuisance	March 25, 2019
Depositions	
Deposition of David Cutler	April 26–27, 2019
Deposition of David Kessler	April 25–26, 2019
Deposition of Holly Woods	September 27, 2018
Deposition of Holly Woods	January 7, 2019
Deposition of Jonathan Gruber	April 25, 2019
Deposition of Margaret June Carr	December 21, 2018
Deposition of Mark Stewart	January 22, 2019
Deposition of Meredith Rosenthal and Errata Sheet	May 4–5, 2019
SEC Filings	
Teva Pharmaceutical Industries Limited, Form 10-K for Fiscal Year Ended December 31, 2017	February 12, 2018
FDA Labels	
FDA, "Actiq©"	November 4, 1998
FDA, "Actiq®"	August 2006
FDA, "Actiq- Fentanyl Citrate Lozenge"	July 2018
FDA, "ACTIQ® (fentanyl citrate) oral transmucosal lozenge, CII"	December 16, 2016

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EXHIBIT 2

Document Title, Bates Numbers	Document Date
FDA, "Fentora® (Fentanyl Buccal Tablet), CII"	December 16, 2016
FDA, "Fentora™"	September 25, 2006
Academic Literature	
Abby Alpert et al., "Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids," *American Economic Journal: Economic Policy* 10, no. 4, pp. 1–35	2018
Alene Kennedy-Hendricks et al., "Opioid Overdose Deaths and Florida's Crackdown on Pill Mills," *American Journal of Public Health* 106, no. 2, pp. 291–297	2016
Alex Hollingsworth et al., "Macroeconomic Conditions and Opioid Abuse," *Journal of Health Economics* 56, pp. 222–233	2017
Amitabh Chandra and Jonathan Skinner, "Technology Growth and Expenditure Growth in Health Care," *Journal of Economic Literature* 50, no. 3, pp. 645–680	2012
Anca M. Grecu et al., "Mandatory Access Prescription Drug Monitoring Programs and Prescription Drug Abuse," *Journal of Policy Analysis and Management* 38, no. 1, pp. 181–209	2019
Andrew Gelman and Jonathan Auerbach, "Age-Aggregation Bias in Mortality Trends," *Proceedings of the National Academy of Sciences* 113, no. 7, pp. E816–E817	2016
Andrew J. Epstein and Jonathan D. Ketcham, "Information Technology and Agency in Physicians' Prescribing Decisions," *The RAND Journal of Economics* 45, no. 2, pp. 422–448	2014
Andrew Rhodes and Chris M. Wilson, "False Advertising," *The RAND Journal of Economics* 49, no. 2, pp. 348–369	2018
Andrew Rosenblum et al., "Opioids and the Treatment of Chronic Pain: Controversies, Current Status, and Future Directions," *Experimental Clinical Psychopharmacology* 16, no. 5, pp. 405–416	2008
Andrew Wilcock and Robert Twycross eds., "Therapeutic Reviews," *Journal of Pain and Symptom Management* 44, no. 1, pp. 131–149	2012
Anne Case and Angus Deaton, "Deaths of Despair Redux: A Response to Christopher Ruhm"	January 8, 2018
Anne Case and Angus Deaton, "Mortality and Morbidity in the 21st Century," Brookings Papers on Economic Activity BPEA Conference Drafts	March 17, 2017
Anne Schuchat et al., "New Data on Opioid Use and Prescribing in the United States," *JAMA* 318, no. 5, pp. 425–426	2017
Anuj Shah et al., "Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015," *CDC Morbidity and Mortality Weekly Report* 66, no. 10, pp. 265–268	March 17, 2017
Anusua Datta and Dhaval Dave, "Effects of Physician-Directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence," *Health Economics* 26, pp. 450–468	2017
Aparna Soni, "Health Insurance, Price Changes, and the Demand for Pain Relief Drugs: Evidence from Medicare Part D," Working Paper	September 25, 2018
Brenda R. Motheral, "Pharmaceutical Step-Therapy Interventions: A Critical Review of the Literature," *Journal of Managed Care Pharmacy* 17, no. 2, pp. 143–155	2011
Burton A. Weisbrod, "The Health Care Quadrilemma: An Essay on Technological Change, Insurance, Quality of Care, and Cost Containment," *Journal of Economic Literature* 29, no. 2, pp. 523–552	1991
C. Lee Ventola, "Off-Label Drug Information: Regulation, Distribution, Evaluation, and Related Controversies," *Pharmacy & Therapeutics* 34, no. 8, pp. 428–449	2009

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EXHIBIT 2

Document Title, Bates Numbers	Document Date
Chao Zhou et al., "Payments for Opioids Shifted Substantially to Public and Private Insurers While Consumer Spending Declined, 1999–2012," *Health Affairs* 35, no. 5, pp. 824–831a	First online in 2016, last updated in 2018
Christopher Jones, "Heroin Use and Heroin Use Risk Behaviors among Nonmedical Users of Prescription Opioid Pain Relievers – United States, 2002–2004 and 2008–2010," *Drug and Alcohol Dependence* 132, pp. 95–100	2013
Christopher M. Wittich et al., "Ten Common Questions (and Their Answers) about Off-Label Drug Use," *Mayo Clinic Proceedings* 87, no. 10, pp. 982–990	2012
Corey S. Davis et al., "Evolution and Convergence of State Laws Governing Controlled Substance Prescription Monitoring Programs, 1998-2011," *American Journal of Public Health* 104, no. 8, pp. 1389–1395	2014
David C. Radley et al., "Off-Label Prescribing among Office-Based Physicians," *Archives of Internal Medicine* 166, pp. 1021–1026	2006
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David Powell et al., "How Increasing Medical Access to Opioids Contributes to the Opioid Epidemic: Evidence from Medicare Part D," Working Paper	April 2017
Davina C. Ling et al., "Deregulation Direct-to-Consumer Marketing of Prescription Drugs: Effects on Prescription and Over-the-Counter Product Sales," *The Journal of Law and Economics* 45, no. S2, pp. 691–723	2002
Deborah Dowell et al., "CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016," *CDC Morbidity and Mortality Weekly Report* 65, no. 1, pp. 1–49	March 18, 2016
Deborah Dowell et al., "Mandatory Provider Review and Pain Clinic Laws Reduce the Amounts of Opioids Prescribed and Overdoes Death Rates," *Health Affairs* 35, no. 10, pp. 1876–1883	2016
Dhaval Dave and Henry Saffer, "Impact of Direct-to-Consumer Advertising on Pharmaceutical Prices and Demand," *Southern Economic Journal* 79, no. 1, pp. 97–126	2012
Douglas E. Mager and Emily R. Cox, "Relationship Between Generic and Preferred-Brand Prescription Copayment Differentials and Generic Fill Rate," *The American Journal of Managed Care* 13, no. 6, pp. 347–352	2007
Edward L. Glaeser and Bruce Sacerdote, "Why Is There More Crime in Cities?" *The Journal of Political Economy* 107, no. S6, pp. S225–S258	1999
E. Ray Dorsey et al., "Impact of FDA Black Box Advisory on Antipsychotic Medication Use," *Archives of Internal Medicine* 170, no. 1, pp. 96–103	2010
Ellen Meara et al., "State Legal Restrictions and Prescription-Opioid Use among Disabled Adults," *The New England Journal of Medicine* 375, no. 1, pp. 44–53	2016
Erin Cavusgil et al, "Late Entrant Over-the-Counter and Rx Market Entry Strategies: An Investigation in the Pharmaceutical Industry," *International Journal of Pharmaceutical and Healthcare Marketing* 5, no. 2, pp. 79–98	2011
Ernst R. Berndt, "To Inform or Persuade? Direct-to-Consumer Advertising of Prescription Drugs," *The New England Journal of Medicine* 352, no. 4, pp. 325–328	2005
Ernst R. Berndt et al., "Information, Marketing, and Pricing in the U.S. Antiulcer Drug Market," *The American Economic Review* 85, no. 2, pp. 100–105	1995
Frank Chaloupka, "Rational Addictive Behavior and Cigarette Smoking," *The Journal of Political Economy* 99, no. 4, pp. 722–742	1991
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Gery P. Guy Jr. et al., "Vital Signs: Changes in Opioid Prescribing in the United States, 2006–2015, *CDC Morbidity and Mortality Weekly Report* 66, no. 26, pp. 697–704	July 7, 2017
Guohua Li et al., "Prescription Drug Monitoring and Drug Overdose Mortality," *Injury Epidemiology* 1, no. 9, pp. 1–8	2014
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James C. Robinson, "Consolidation and the Transformation of Competition in Health Insurance," *Health Affairs* 23, no. 6, pp. 11–24	2004
James H. Stock and Mark W. Watson, *Introduction to Econometrics*, Third Edition (Boston, MA: Addison-Wesley)	2011
Jane C. Ballantyne and Jianren Mao, "Opioid Therapy for Chronic Pain," *The New England Journal of Medicine* 349, no. 20, pp. 1943–1953	2003
Jay M. Margolis et al., "Effects of a Medicaid Prior Authorization Policy for Pregabalin," *The American Journal of Managed Care* 15, no. 10, pp. e95–e102	2009
Jean-Pierre Dubé et al., "An Empirical Model of Advertising Dynamics," *Quantitative Marketing and Economics* 3, pp. 107–144	2005
Jeffrey M. Wooldridge, *Introductory Econometrics: A Modern Approach*, Fifth Edition (Mason, OH: South-Western)	2013
Joanne E. Brady et al., "Prescription Drug Monitoring and Dispensing of Prescription Opioids," *Public Health Reports* 129, pp. 139–147	2014
John A. Rizzo, "Advertising and Competition in the Ethical Pharmaceutical Industry: The Case of Antihypertensive Drugs," *The Journal of Law and Economics* 42, no. 1, pp. 89–116	1999
John Bian et al., "Effects of the US Food and Drug Administration Boxed Warning of Erythropoietin-Stimulating Agents on Utilization and Adverse Outcome," *Journal of Clinical Oncology* 35, no. 17, pp. 1945–1951	2017
John Cawley et al., "The Effect of Deceptive Advertising on Consumption of the Advertised Good and Its Substitutes: The Case of Over-the-Counter Weight Loss Products," NBER Working Paper No. 18863	March 2013
John K. Gorman et al., "Chapter 24: Health Plans and Medicare" in *Essentials of Managed Health Care,* Sixth Edition, ed. Peter R. Kongstvedt (Burlington, MA: Jones & Bartlett Learning), pp. 501–506	2013
Jonathan D. Ketcham and Andrew J. Epstein, "Which Physicians are Affected Most by Medicaid Preferred Drug Lists for Statins and Antihypertensives?" *Pharmacoeconomics* 24, no. 3, pp. 27–40	2006
Jonathan D. Ketcham and Kosali I. Simon, "Medicare Part D's Effects on Elderly Patients' Drug Costs and Utilization," *American Journal of Managed Care* 14, no. 11, pp. SP14–SP22	2008
Jonathan Gruber and Botond Köszegi, "Is Addiction 'Rational'? Theory and Evidence," *The Quarterly Journal of Economics* 116, no. 4, pp. 1261–1303	2001
Jonathan Skinner and Douglas Staiger, "Technology Diffusion and Productivity Growth in Health Care," *The Review of Economics and Statistics* 97, no. 5, pp. 951–964	2015
Joseph P. Newhouse, "Medical Care Costs: How Much Welfare Loss?" *Journal of Economic Perspectives* 6, no. 3, pp. 3–21	1992

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U.S. Census Bureau American Community Survey Questionnaire	2019
U.S. Census Bureau Current Population Survey Health Insurance Coverage Tables	1999 – 2012

EXHIBIT 2

Document Title, Bates Numbers	Document Date
Miscellaneous	
Anuj Shah et al. (2017) table, "One- and 3-year probabilities of continued use, and median time to discontinuation of opioid use, by choice of first opioid prescription"	2017
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Jonathan D. Rockoff and Ron Winslow (2013) chart, "Off to a Slower Start: New drug launches in the U.S. in recent years haven't been as successful as they had been"	December 15, 2013
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Note: In addition to the documents on this list, I considered all documents cited in my report and my exhibits to form my opinions.

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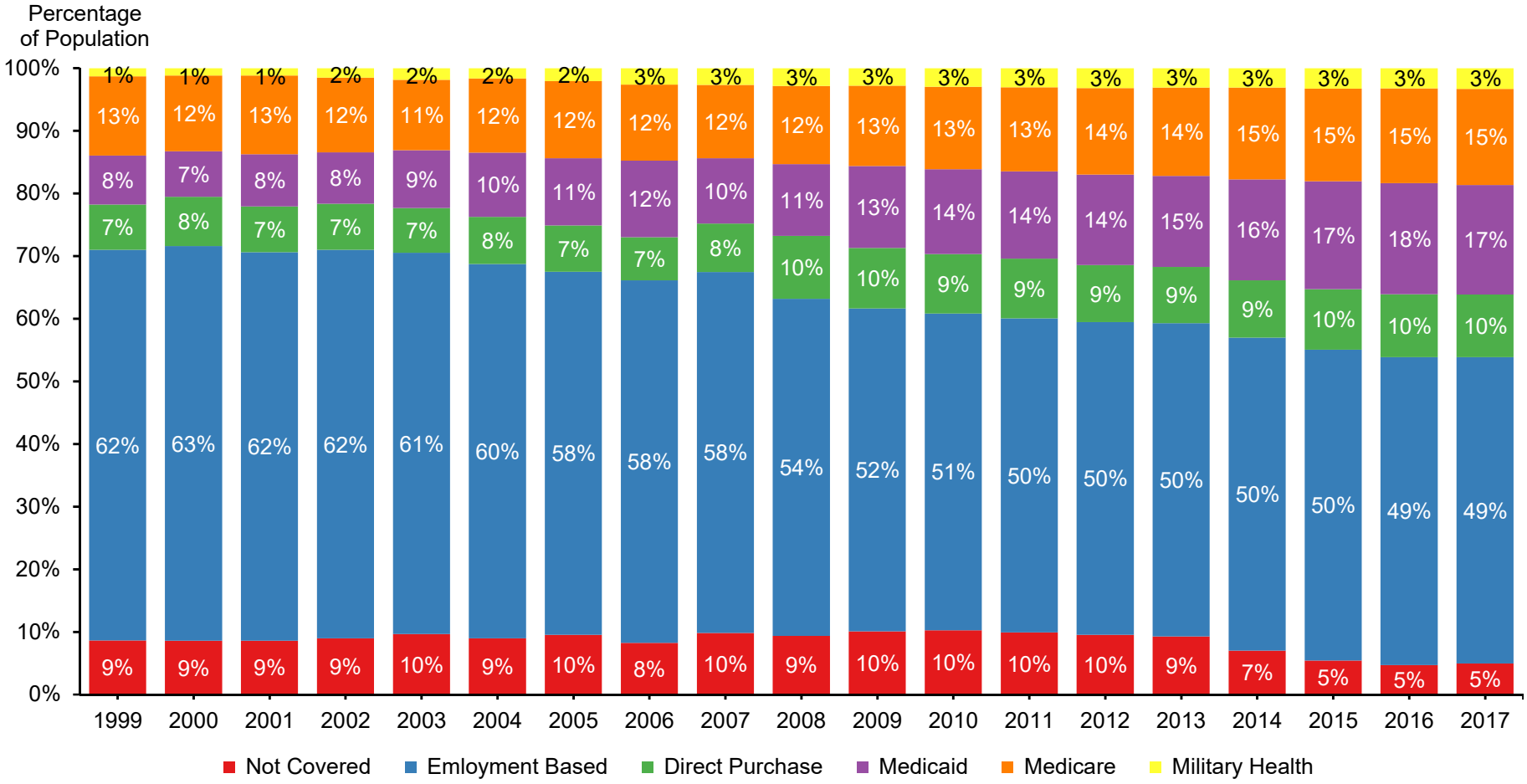
EXHIBIT 3

Ohio Population by Type of Insurance Coverage
1999 – 2017

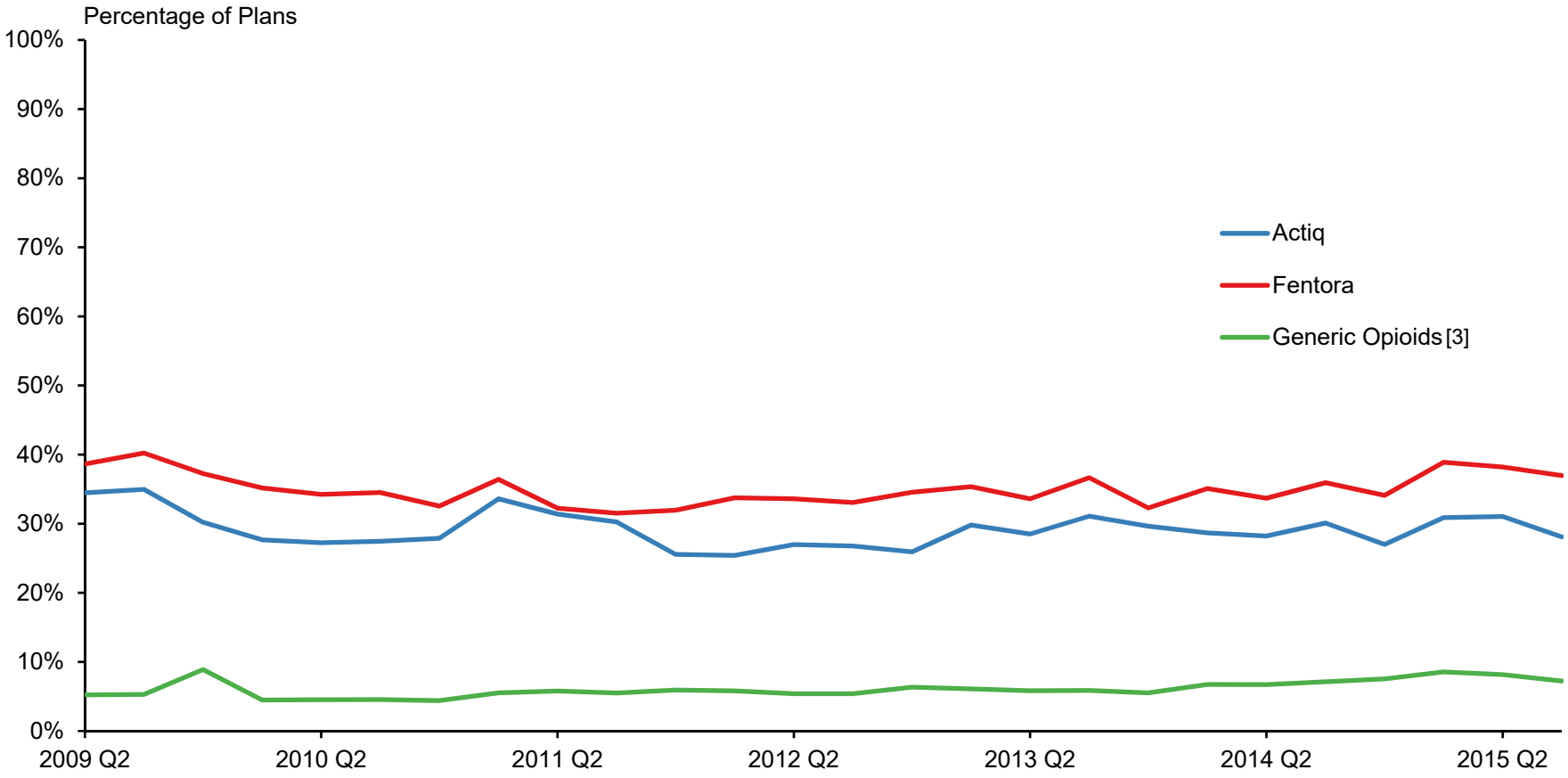


Source: U.S. Census Bureau, 1-year American Community Survey; U.S. Census Bureau, Current Population Survey; The American Community Survey 2019 Questionnaire

Note: For the years 1999 to 2007 I use the data from the Current Population Survey, while for the years 2008 to 2017 I use the data from the American Community Survey. The type of insurance coverage categories in the Current Population Survey and the American Community Survey are not mutually exclusive, therefore population is assumed to be equal to the sum of the number of individuals counted in each type of insurance coverage category presented in the above chart. The category "Employment Based" refers to insurance through a current or former employer or union of the individual or another family member. The category "Direct Purchase" refers to insurance purchased directly from an insurance company by the individual or another family member. The category "Military health" includes Tricare, Veterans Administration, and military health care.

EXHIBIT 4

Ohio Formulary Placement
Percentage of Plans Where Selected Opioids Require Prior Authorization
2nd Quarter 2009 – 3rd Quarter 2015[1][2]



Source: Fingertip Formulary Data

Note:

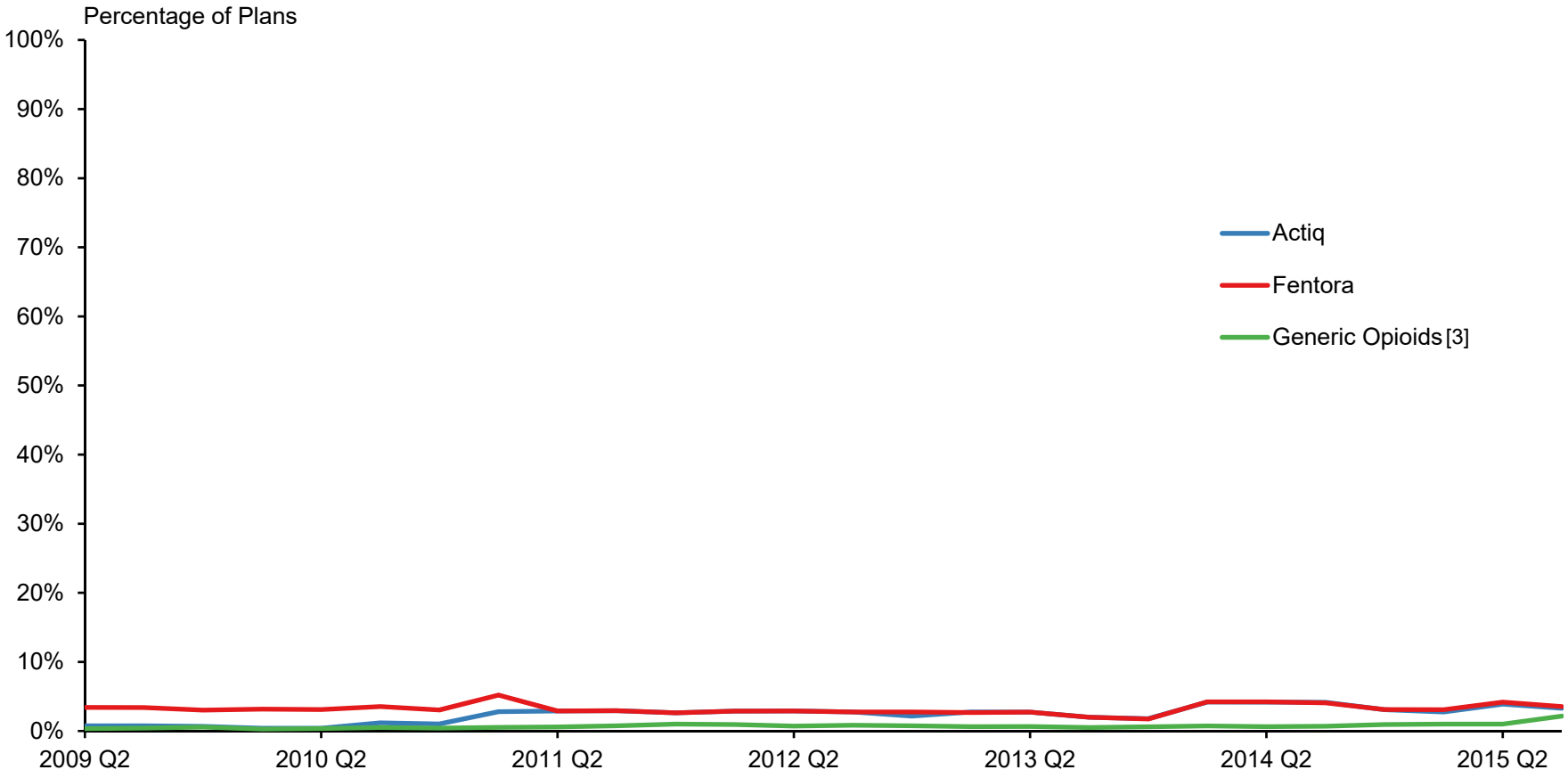
[1] I include all health plans operating in Ohio in a given quarter except the State of Ohio Medicaid plan administered by the Ohio Department of Medicaid.

[2] If a drug is not mentioned in a given plan's formulary, the plan-drug pair does not factor into the percentage of plans that require prior authorization.

[3] I restrict attention to those generic opioids for which the Teva or Actavis Generic Defendants manufacture a version. I exclude tramadol because Fingertip Forumlary data does not distinguish between branded and generic tramadol before 2012.

EXHIBIT 5

Ohio Formulary Placement
Percentage of Plans Where Selected Opioids Require Step Therapy
2nd Quarter 2009 – 3rd Quarter 2015[1][2]



Source: Fingertip Formulary Data

Note:

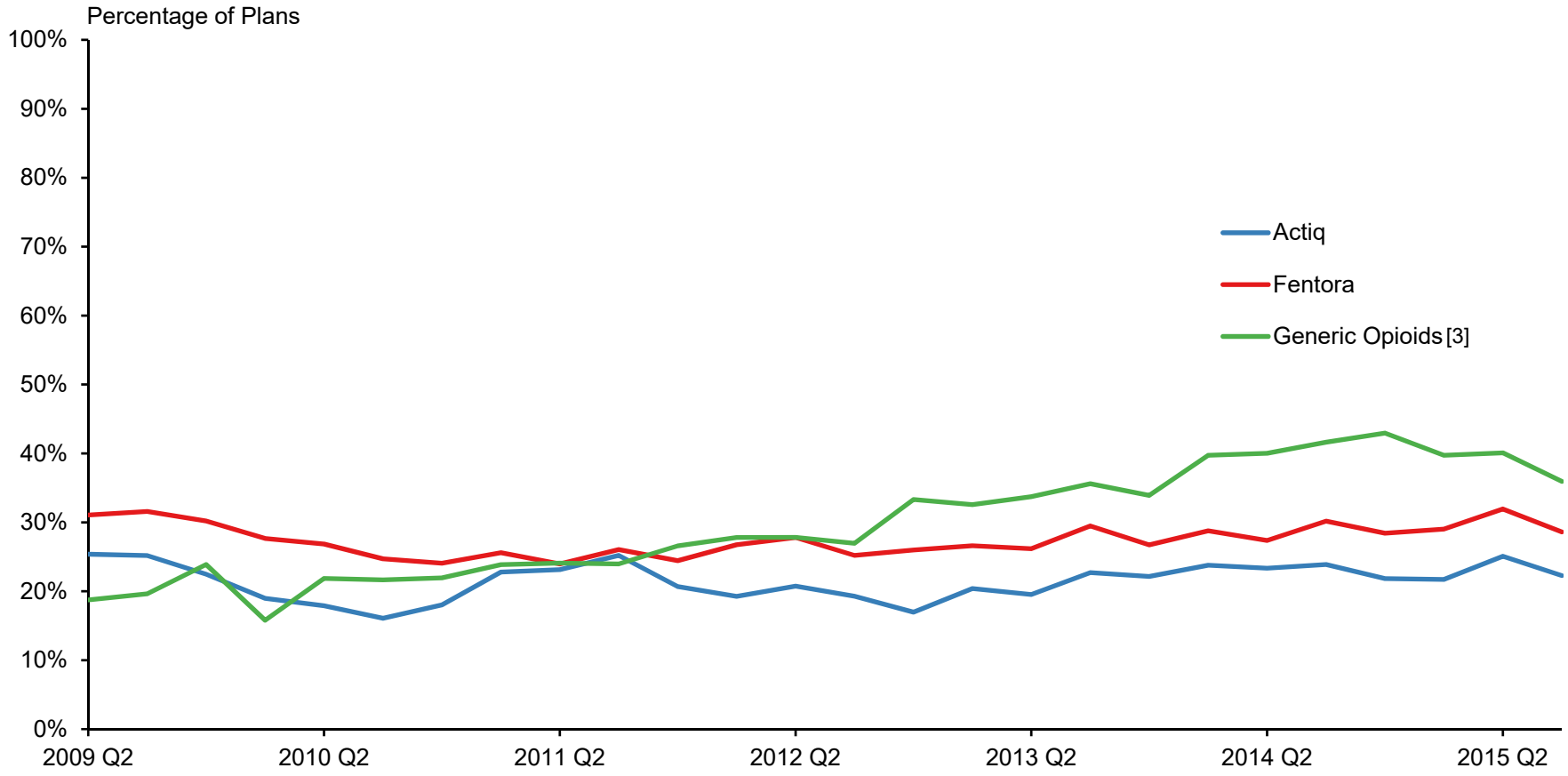
[1] I include all health plans operating in Ohio in a given quarter except the State of Ohio Medicaid plan administered by the Ohio Department of Medicaid.

[2] If a drug is not mentioned in a given plan's formulary, the plan-drug pair does not factor into the percentage of plans that require step therapy.

[3] I restrict attention to those generic opioids for which the Teva or Actavis Generic Defendants manufacture a version. I exclude tramadol because Fingertip Forumlary data does not distinguish between branded and generic tramadol before 2012.

EXHIBIT 6

Ohio Formulary Placement
Percentage of Plans Where Selected Opioids Have Quantity Limits
2nd Quarter 2009 – 3rd Quarter 2015[1][2]



Source: Fingertip Formulary Data

Note:

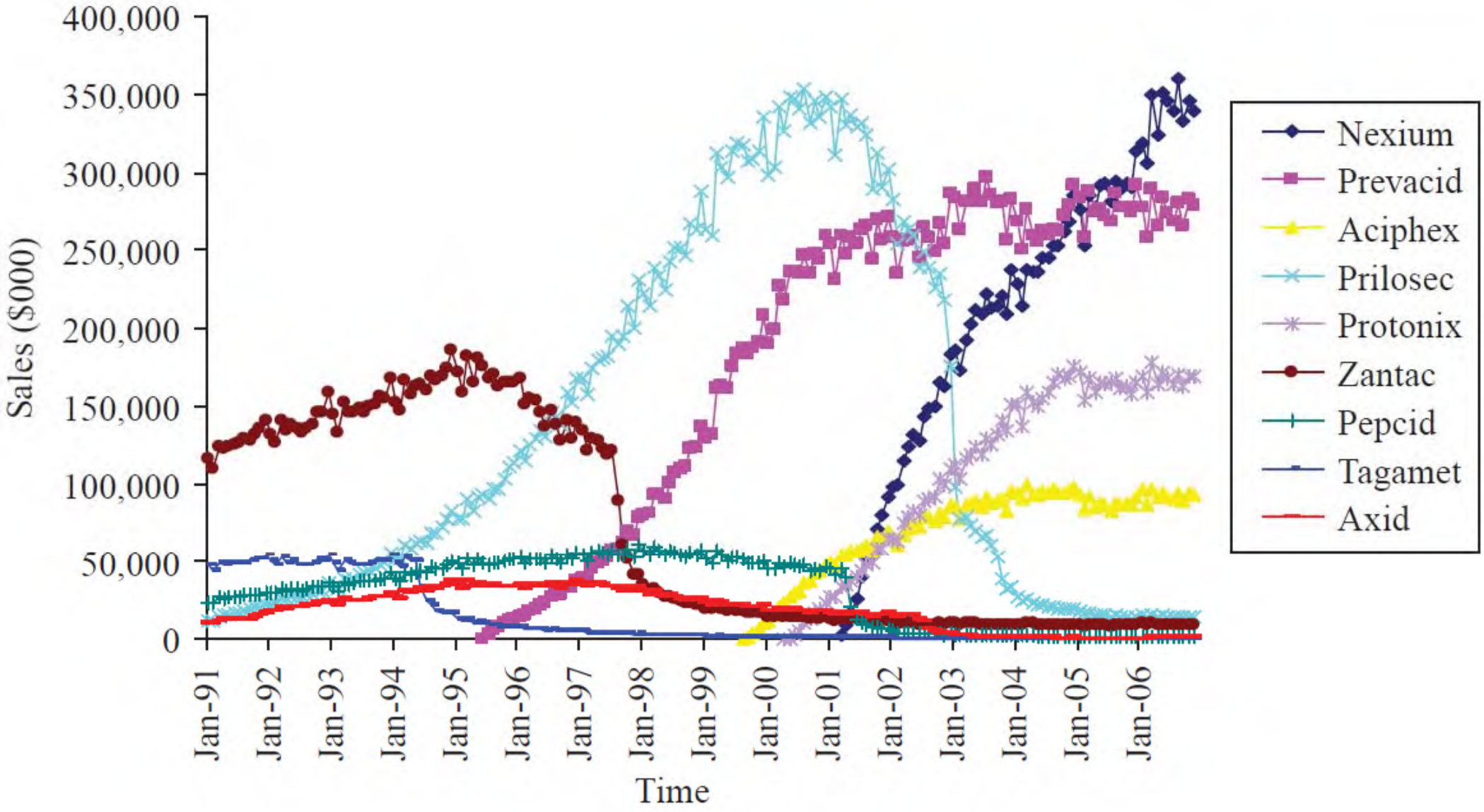
[1] I include all health plans operating in Ohio in a given quarter except the State of Ohio Medicaid plan administered by the Ohio Department of Medicaid.

[2] If a drug is not mentioned in a given plan's formulary, the plan-drug pair does not factor into the percentage of plans that have quantity limits.

[3] I restrict attention to those generic opioids for which the Teva or Actavis Generic Defendants manufacture a version. I exclude tramadol because Fingertip Forumlary data does not distinguish between branded and generic tramadol before 2012.

EXHIBIT 7

EXHIBIT 8



Source: Erin Cavusgil et al, "Late Entrant Over-the-Counter and Rx Market Entry Strategies: An Investigation in the Pharmaceutical Industry," *International Journal of Pharmaceutical and Healthcare Marketing* 5, no. 2, 2011, pp. 79–98

EXHIBIT 9

Validation Test Using Randomly Generated Sets of Numbers in Place of Detailing [1][2]

Parameter [4]	Professor Rosenthal's Model B [3]		Summary Statistics Across 1,000 Iterations of This Validation Test					
	Estimate	Statistical Significance [5]	Minimum	2.5th Percentile	Average	97.5th Percentile	Maximum	Percentage of Iterations with Statistical Significance [6]
Constant (in millions)	2,447	***	844	1,152	1,622	2,052	2,314	100%
Stock of Random Numbers * Sub Period 1 Dummy	934	***	528	586	677	777	873	100%
Stock of Random Numbers * Sub Period 2-3 Dummy	1,111	***	669	755	861	985	1,123	100%
Stock of Random Numbers * Sub Period 3 Dummy Trend	-7.974	***	-8.017	-7.186	-6.330	-5.593	-4.943	100%
Depreciation Rate Constant	-0.0067	***	-0.0070	-0.0066	-0.0059	-0.0052	-0.0047	100%
Aggregate Price Index (in millions)	-1,947	***	-1,781	-1,504	-1,096	-688	-426	98%
R-Squared	0.9937		0.9927	0.9931	0.9936	0.9940	0.9942	

Source: Rosenthal Expert Report and Production Materials

Note:

[1] The random numbers could take on a uniform value between 0 and 100. For ease of comparison to Professor Rosenthal's results presented in Table 1 of her expert report, they were multiplied by 1,000.

[2] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.

[3] Professor Rosenthal's Results as Presented in Table 1 of her expert report.

[4] The minimum, maximum and percentile values reported for the parameters correspond to the minimum, maximum and percentile values of the specified parameter across the 1,000 sets of outputs.

[5] "***" Reflects statistical significance at the 99% confidence level.

[6] Statistical significance is determined at the 95% confidence level.

EXHIBIT 10

EXHIBIT 11

Validation Test Using the Price of Gold as the Dependent Variable [1]

Parameter	Estimate	Statistical Significance [2]
Constant	1,545	***
Stock of Detailing Contacts * Sub Period 1 Dummy	1.097E-05	***
Stock of Detailing Contacts * Sub Period 2-3 Dummy	2.374E-05	***
Stock of Detailing Contacts * Sub Period 3 Dummy Trend	-2.054E-07	***
Depreciation Rate Constant	-0.01586	***
Aggregate Price Index	-1,159	***
R-Squared	0.9494	
Sub Period 1	Jan '93 – Dec '02	
Sub Period 2	Jan '03 – Nov '11	
Sub Period 3	Dec '11 – May '18	

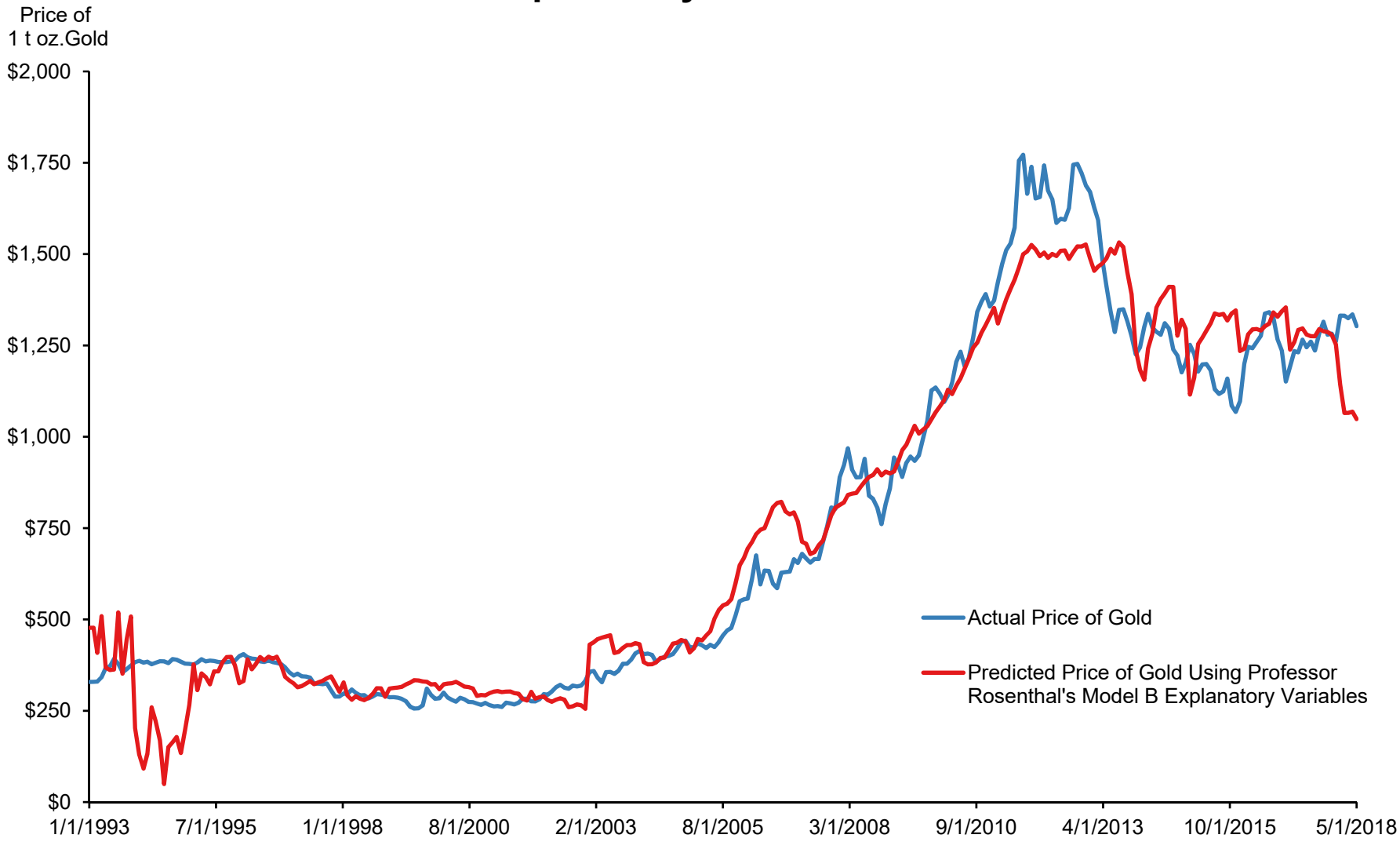
Source: Rosenthal Expert Report and Production Materials; Federal Reserve Economic Data
Note:

[1] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.

[2] "***" Reflects statistical significance at the 99% confidence level.

EXHIBIT 12

Price of Gold Predicted by Professor Rosenthal's Model B and Her Explanatory Variables [1]



Source: Rosenthal Expert Report and Production Materials; Federal Reserve Economic Data

Note:

[1] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.

EXHIBIT 13

Validation Test Based on Using Detailing Only Prior to March 2002 [1]

Parameter	Estimate	Statistical Significance [2]
Constant *(in millions)*	2,550	***
Stock of Pre-March 2002 Detailing Contacts * Sub Period 1 Dummy	840	***
Stock of Pre-March 2002 Detailing Contacts * Sub Period 2-3 Dummy	1,047	***
Stock of Pre-March 2002 Detailing Contacts * Sub Period 3 Dummy Trend	-7.991	***
Depreciation Rate Constant	-0.0091	***
Aggregate Price Index *(in millions)*	-2,018	***
R-Squared	0.9936	
Sub Period 1	Jan '93 – Jun '02	
Sub Period 2	Jul '02 – Sep '10	
Sub Period 3	Oct '10 – May '18	

Source: Rosenthal Expert Report and Production Materials
Note:
[1] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.
[2] "***" Reflects statistical significance at the 99% confidence level.

EXHIBIT 14

EXHIBIT 15

Results of Professor Rosenthal's Model B Using Various Depreciation Rates [1]

	δ = -.0067		δ = 0.05		δ = 0.1		δ = 0.2		δ = 0.3		δ = 0.4	
Parameter	**Estimate**	**Statistical Significance [2]**	**Estimate**	**Statistical Significance [2]**	**Estimate**	**Statistical Significance [2]**	**Estimate**	**Statistical Significance [2]**	**Estimate**	**Statistical Significance [2]**	**Estimate**	**Statistical Significance [2]**
Constant *(in millions)*	2,447	***	-21,435	***	-20,649	***	-18,786	***	-17,618	***	-16,906	***
Stock of Detailing Contacts * Sub Period 1 Dummy	934	***	-6,434	***	-9,806	***	-14,030	***	-16,455	***	-18,873	**
Stock of Detailing Contacts * Sub Period 2-3 Dummy	1,111	***	-1,216	*	223		6,809	**	15,927	***	25,366	***
Stock of Detailing Contacts * Sub Period 3 Dummy Trend	-7.974	***	-621	***	-1,320	***	-2,445	***	-3,341	***	-4,171	***
Aggregate Price Index *(in millions)*	-1,947	***	24,762	***	23,552	***	21,233	***	19,778	***	18,926	***
R-Squared	0.9937		0.9133		0.8915		0.8608		0.8429		0.8329	
Sub Period 1	Jan '93 – Feb '02		Jan '93 – Dec '98		Jan '93 – Dec '98		Jan '93 – Dec '98		Jan '93 – Dec '98		Jan '93 – Dec '98	
Sub Period 2	Mar '02 – Jul '10		Jan '99 – Nov '11		Jan '99 – Nov '11		Jan '99 – Nov '11		Jan '99 – Nov '11		Jan '99 – Nov '11	
Sub Period 3	Aug '10 – May '18		Dec '11 – May '18		Dec '11 – May '18		Dec '11 – May '18		Dec '11 – May '18		Dec '11 – May '18	

Source: Rosenthal Expert Report and Production Materials

Note:

[1] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.

[2] "***" Reflects statistical significance at the 99% confidence level. "**" Reflects statistical significance at the 95% confidence level. "*" Reflects statistical significance at the 90% confidence level.

EXHIBIT 16

Correlation Between Professor Rosenthal's Indirect Approach Excess MMEs and Stock of Detailing Using Various Depreciation Rates [1]

Depreciation Rate Used for Stock of Detailing [2]	Correlation Between Stock of Detailing and Excess MMEs
δ = -0.0067	0.8380
δ = 0.05	0.1201
δ = 0.10	0.0097
δ = 0.20	0.0051
δ = 0.30	0.0044
δ = 0.40	0.0028

Source: Rosenthal Expert Report and Production Materials
Note:
[1] Excess MMEs are calculated using Professor Rosenthal's production code, which calculates the excess shipments in MMEs displayed in Table 5 of her report. The stock of detailing was calculated using Professor Rosenthal's methodology and data.
[2] The unit of analysis for computing the correlation is a year. Excess MMEs calculated using Professor Rosenthal's indirect approach for a year are compared with the average stock of detailing for the nation during that year.

EXHIBIT 17

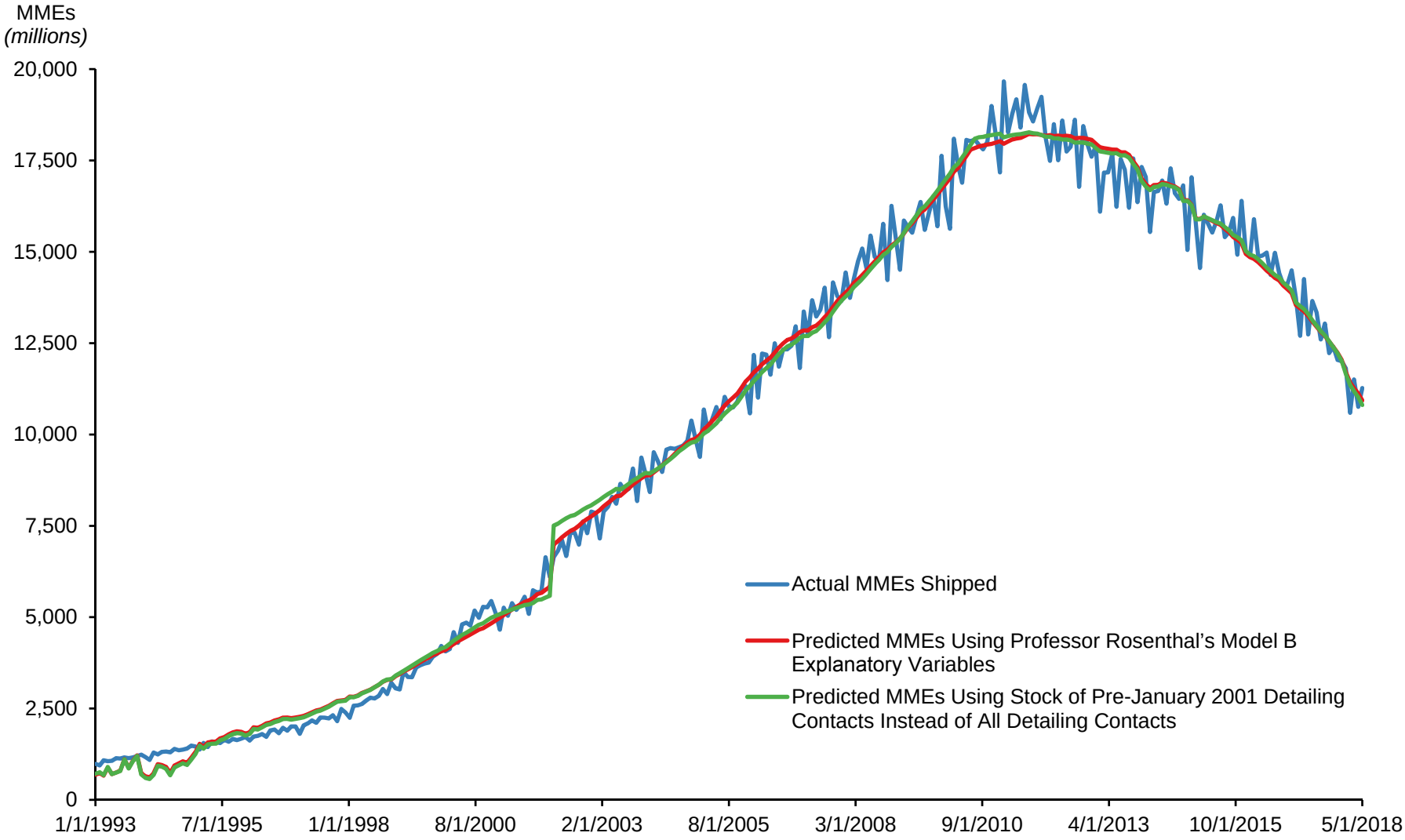
Validation Test Based on Using Detailing Only Prior to January 2001[1]

Parameter	Estimate	Statistical Significance[2]
Constant *(in millions)*	2,554	***
Stock of Pre-January 2001 Detailing Contacts * Sub Period 1 Dummy	841	***
Stock of Pre-January 2001 Detailing Contacts * Sub Period 2-3 Dummy	1,131	***
Stock of Pre-January 2001 Detailing Contacts * Sub Period 3 Dummy Trend	-8.608	***
Depreciation Rate Constant	-0.0093	***
Aggregate Price Index *(in millions)*	-2,029	***
R-Squared	0.9935	
Sub Period 1	Jan '93 – Feb '02	
Sub Period 2	Mar '02 – Aug '10	
Sub Period 3	Sep '10 – May '18	

Source: Rosenthal Expert Report and Production Materials
Note:
[1] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.
[2] "***" Reflects statistical significance at the 99% confidence level.

EXHIBIT 18

Professor Rosenthal's Model B Predicted MMEs Assuming Flow of Detailing Stopped in January 2001[1]



Source: Rosenthal Expert Report and Production Materials

Note:

[1] Professor Rosenthal's Model B methodology and data (when relevant) were used to determine the coefficients, the different sub periods, and statistical significance. The same time period was also used to perform the regression analysis, 1/1/1993 – 5/1/2018.

Errata to May 10, 2019 Expert Report of Jonathan Ketcham, PhD

Page	Paragraph	Line(s)	Footnote	Line(s)	Change From	Change To
2			1	2	May 18, 2018	May 25, 2018
17			76	1	Original Actiq Label, p. 53	FDA, Actiq Label, August 2006
22	53	5			See Section IV.A	See ¶ 161.
27	66				paragraph 66	move between paragraphs 99 and 100
35	90				90. According to Fingertip Formulary data Ohio Medicaid fee-for-service had PA restrictions in place for Actiq and Fentora throughout the period considered in my analysis. However, for the majority of the period considered, more than half of generics manufactured by the Teva and Actavis Generic Defendants had no PA restrictions in place. In fact, in the first quarter of 2010 more than 80 percent of the Teva and Actavis Generic Defendants' generic opioids did not require prior authorization. Even through the third quarter of 2015, more than 40 percent of generic opioids were available without prior authorization. This limited use of PA by third party health plans shows that these parties could have taken but failed to take more aggressive measures to curb opioid prescriptions.	90. According to Fingertip Formulary data Ohio Medicaid fee-for-service had PA restrictions in place for Actiq and Fentora throughout the period considered in my analysis. However, for the majority of the period considered, Ohio Medicaid had no restrictions in place for more than half of generics manufactured by the Teva and Actavis Generic Defendants. In fact, in the first quarter of 2010, Ohio Medicaid did not require prior authorization for more than 80 percent of the Teva and Actavis Generic Defendants' generic opioids. Even through the third quarter of 2015, more than 40 percent of generic opioids were available without prior authorization. This limited use of PA by third party health plans shows that these parties could have taken but failed to take more aggressive measures to curb opioid prescriptions.
47			236	1	2018	2017
47			238	1	2018	2017
54			272	1	See Section **Error! Reference source not found.** above.	See Section V.C.
55			280	1	Dave and Saffer (2012), p. 107.	Dhaval Dave and Henry Saffer, "Impact of Direct-to-Consumer Advertising on Pharmaceutical Prices and Demand," *Southern Economic Journal* 79, no. 1, 2012 ("Dave and Saffer (2012)"), pp. 97–126 at p. 107.
56			282	1	Mizik and Jacobson (2004), at p. 1704.	Natalie Mizik and Robert Jacobson, "Are Physicians 'Easy Marks'? Quantifying the Effects of Detailing and Sampling on New Prescriptions," *Management Science* 50, no. 12, 2004 ("Mizik and Jacobson (2004)"), pp. 1704–1715 at p. 1704.
59			298	2	NBER, May 15, 2018	NBER Working Paper No. 24468, May 15, 2018

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Page	Paragraph	Line(s)	Footnote	Line(s)	Change From	Change To
76	197				Add to end of paragraph	The same results hold true if we calculate detailing stock assuming no detailing happened after January 1, 2001. These results are shown in Exhibits 17 and 18. Again, the implication is that, following Professor Rosenthal's logic, detailing prior to January 1, 2001 caused opioid shipments for the period 1995-2018.
78			379	1	Chaloupka (1999)	Chaloupka (1991)
79	209				As explained in Section IV	As explained in Section II
87			413	3–4	Robert Wood Johnson Foundation Research Synthesis Report 18, 2008	The Synthesis Project, Robert Wood Johnson Foundation, Research Synthesis Report No. 16, October 2008
90			421	1	Rosenthal Report, Attachment D	Rosenthal's production code "Indirect_regressions_w_adj_st_final.sas."
List of Documents Ccnsidered p.1					Deposition of Mark Stewart January 22, 2019	Delete

Jonathan Ketcham, PhD, 5/28/2019